(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 16 August 2001 (16.08.2001)

PCT

(10) International Publication Number WO 01/58951 A2

(51) International Patent Classification7:

. - -

(21) International Application Number: PCT/EP01/01457

(22) International Filing Date: 9 February 2001 (09.02.2001)

(25) Filing Language:

English

C07K 14/705

(26) Publication Language:

English

(30) Priority Data:

00200443.0 00203810.7 10 February 2000 (10.02.2000) EP 31 October 2000 (31.10.2000) EP

(71) Applicant (for all designated States except US): STICHT-ING VOOR DE TECHNISCHE WETENSCHAPPEN [NL/NL]; Van Vollenhovenlaan 661, NL-3527 JP Utrecht (NL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): SMIT, August, Benjamin [NL/NL]; Achillesstraat 28 II, NL-1076 RC Amsterdam (NL). SIXMA, Titia, Karen [NL/NL]; Ingen Houszstraat 61, NL-3514 HV Utrecht (NL).

(74) Agent: VOSSIUS & PARTNER; Siebertstr. 4, D-81675 München (DE).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

 without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

A2

(54) Title: WATER-SOLUBLE LIGAND-BINDING PROTEINS AND ANALOGS OF LIGAND-GATED ION CHANNELS, CRYSTALS THEREOF AND THEIR USE FOR SCREENING LIGANDS OF LIGAND-GATED ION CHANNELS

(57) Abstract: Provided are water-soluble ligand-binding proteins derived from molluscs and analogs of ligand-gated ion channels, crystals thereof and their use for screening ligands of ligand-gated ion channels. In particular, water-soluble ligand-binding proteins are provided that are capable of forming multimers and are amenable to crystallization. The crystal structure of one of these proteins, an acetylcholine binding protein (AChBP) is provided, which can be used to generate 3D models of the extracellular ligand-binding domain of ligand-gated ion channels and thus for screening of drugs that act on these ion channels. Furthermore, chimeric proteins are provided that are capable of binding a ligand of a ligand-gated receptor, and comprising at least the amino acids of the AChBP determining solubility of the AChBP, in the same positions as in the AChBP, and furthermore comprising amino acids determining binding to said ligand.

WO 01/58951

PCT/EP01/01457

WATER-SOLUBLE LIGAND-BINDING PROTEINS AND ANALOGS OF LIGAND-GATED ION CHANNELS, CRYSTALS THEREOF AND THEIR USE FOR SCREENING LIGANDS OF LIGAND-GATED ION CHANNELS

10

15

20

25

30

35

5

SUMMARY OF THE INVENTION.

Novel water-soluble ligand-binding proteins have been identified and isolated, which have a ligand-binding profile substantially similar to that of ligand-gated ion channels. DNA molecules encoding such proteins have been cloned and characterized. The biological and structural properties of these proteins are disclosed, as is the amino acid and nucleotide sequence. The recombinant DNA molecules, and portions thereof, are useful for isolating homologues of the DNA molecules, identifying and isolating genomic equivalents of the DNA molecules, and identifying, detecting or isolating mutant forms of the DNA molecules. Using a recombinant expression system functional DNA molecules encoding the water-soluble ligand-binding proteins as well as chimeras have been functionally produced. Furthermore, the water-soluble ligand-binding proteins could be crystallized revealing the three dimensional (3D) structure and enabling the modeling of the 3D structure of the ligand-binding domain of ligand-gated ion channels. The invention is further in the field of the development of new drugs that are capable of selectively intervening in neuronal signaling pathways. The invention is more in particular concerned with providing new analogues of the channel-coupled receptors, crystal structures thereof and to their use in screening ligands for these receptors.

Several documents are cited throughout the text of this specification either by name or are referred to by numerals within parenthesis. Full bibliographic citations may be found at the end of the specification immediately preceding the claims. Each of the documents cited herein (including any manufacturer's specifications, instructions, etc.) are hereby incorporated herein by reference; however, there is no admission that any document cited is indeed prior art as to the present invention.

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-2

BACKGROUND OF THE INVENTION

The communication in the central nervous system (CNS) occurs through a complex interaction of electrical and chemical signals. Molecules bearing chemical information are called neurotransmitters. The chemical information is converted in electric currents on the post-synaptic membrane, which is specialised in recognising and binding neurotransmitters by means of protein receptors. The specific binding of a ligand to one type of such receptors, the ionotropic receptors, induces a fast opening of the ion channel coupled to the receptor. An important group of ionotropic receptors is the superfamily of the channel-coupled receptors, also referred to as ligand-gated receptors, including the 7-amino-butyric acid (GABA_A) receptor, the glycine receptor, the serotonin-3 (5-HT3) receptor and both neuronal and muscle-type nicotinic acetylcholine receptors (nAChR). These receptors share certain structural features such as (1) a 15-residue cysteine loop between amino acids 128 and 142 corresponding to the Torpedo AChR α unit, (2) four trans-membrane domains, (3) similar subunit arrangements, and (4) homologies in amino acid sequence. Activation of these receptors causes a change in electrical current and hyperpolarisation of the cell membrane and consequently an inhibition of the electrical activity of the cell. The GABA_A receptor and the glycine receptor are coupled to a chloride-selective channel, and thus the inhibition of the electrical activity leads to inhibition of the cell response. On the other hand, activation of the 5-HT3 receptor and the nAChRs provokes an excitatory response on the cell because they are connected to a cation-selective channel (Na+, K+, Ca2+). The AChRs are the best studied of the ligand-gated receptors; for a review, see Arias, Brain Research Reviews, 25 (1997)133-191 and Arias, Neurochem, Int. 36 (2000), 595-645). Mutations in these ligand-gated ionchannels (LGICs) lead to diseases such as congenital myasthenia gravis, epilepsy, startle syndrome and alcohol sensitivity (Vafa and Schofield, Int. Rev. Neurobiol. 42, 285-332; 1998). NAChRs mediate nicotine addiction in chronic tobacco users. Since nicotine binding to these receptors also has a positive effect on Alzheimer's disease, Parkinson's disease and schizophrenia these receptors present an important drug target (Paterson and Nordberg, A. Neuronal nicotinic receptors in the human brain. Prog. Neurobiol. 61, 75-111; 2000).

The development of new active compounds that can selectively or - as the case may be - a-selectively bind to the channel-coupled receptors, is of utmost importance for the understanding of the processes occurring in the nervous system and for the treatment of disturbances of neural conditions. The development of such active compounds requires the availability of a reliable model system for the corresponding receptors. The primary structural features (amino acid sequences) of the various

20

25

30

35

WO 01/58951 PCT/EP01/01457

receptors have been largely elucidated by now. Certain subunits of the AChRs have been found to be determinant in the pharmacological specificity or affinity of the receptor for its ligand (Corringer et al., J. Neuroscience 18 (1998), 648-657). However, the study of the ligand binding properties of the receptor proteins is hampered by the fact that the spatial structure of the proteins - which is decisive in the binding of ligands - is still unknown. This is partly because crystallisation of the receptor proteins has been unsuccessful up to now.

The above-defined technical problem is solved by the present invention by providing the embodiments characterized in the claims.

Accordingly, in one aspect the present invention relates to a water-soluble protein derived from a mollusc being capable of binding a ligand of a ligand-gated receptor.

It has been found according to the invention that acetylcholine-binding proteins (AChBP) of certain molluses show a surprising structural similarity with the channel-coupled receptors on the one hand and have interesting physical properties, such as water-solubility, on the other hand. The molluscan AChBPs are capable of forming multimers, especially pentamers, and of binding specific toxins such as α -bungarotoxin. These multimers may be homogeneous (identical units) or heterogeneous (different units). These properties make them eminently suitable as model systems for studying the binding of candidate ligands to the channel-coupled receptors. It has been possible to produce these molluscan AChBPs in recombinant systems, thus allowing convenient and large-scale production thereof. Moreover, it is feasible to construct hybrid proteins sharing the physical properties of the mollusc AChBP with the pharmacological properties of the (human) channel-coupled receptors, thus providing new dedicated tools for screening ligands for these receptors.

The AChBP is a naturally occurring analogue of the extracellular domains of the α -subunits of the neuronal nicotinic acetylcholine receptors (nAChRs). In contrast to the nAChRs, it lacks domains to form a transmembrane ion channel, but alike the nAChRs it assembles into a homo-pentamer (Figure 6). Moreover, AChBP has ligand-binding characteristics that are typical for a nicotinic receptor. The 3-dimensional structure of AChBP was solved by X-ray crystallography at 2.7Å resolution (current R_{tactor} = 27.9 %, R_{tree} = 30.0 %). In crystals, as in solution, AChBP forms a stable homo-pentamer with dimensions comparable to those of the ligand-binding domain of the nAChR, as determined in EM studies by Unwin, Struct. Struct. Biol 121 (1998), 181-190. The high-resolution crystal structure of AChBP, along with

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-4

biochemical and pharmacological data, supports the extrapolation of AChBP as a good mimic of ligand-binding domains of ligand-gated ion channels including nAChR, 5-HT3R, GABA_{AC}R and GlyR.

Four AChBPs according to the present invention are exemplified herein, isolated and cloned from the CNS of Lymnaea stagnalis (L-AChBP_T1 and L-AChBP_T2) and Bulinus truncatus (B-AChBP_T1 and B-AChBP_T2). L-AChBP_T1 and 2 are 229 amino acid proteins with a signal sequence of 19 amino acids (224 and 21 amino acids, respectively, for B-AChBP_T1 and 2; see also Figure 1) and have sequence homology with the extracellular domains of the subunits of ligand-gated ion channels (Figure 3), in particular with those of the nAChRs (Figure 4 and 5). The mass of the purified AChBP from Lymnaea has been determined by mass-spectrometry. The glycosylated form has a mass of about 24720 Da and the de-glycosylated form of about 23832 Da. In SDS-PAGE the glycosylated AChBP migrates between the 14 and 26 kDA marker proteins. Hydrophopicity plots of the AChBPs are shown in Figure 2, which reveal those regions of the ligand-binding proteins that are particularly hydrophilic and thus may be replaced at least in part or essential amino acids thereof in the ligand-binding domain of the ligand-gated ion channel. Sequence conservation is particularly high in the so-called loop areas (reviewed by Arias, Neurochem. Int. 36 (2000), 595-645), which contain the residues involved in ligandbinding. The cysteine residues characteristic for the Cys-loop family of ligand gated receptors are conserved in AChBP. Also the double cysteine typically found in the alpha subunits of the nAChR is present. AChBP protein sequence ends at the position where in the nAChRs the first predicted transmembrane domain would start. The ligand-binding characteristics of AChPBs are described in Example 4 and summerized in Table 2.

The terms "channel coupled receptors", "ligand-gated receptor", "ligand-gated ion channel" are used interchangeable herein. However, in context with the natural occurring, in particular human molecules the term "ligand-gated ion channel" is preferably used. The water-soluble ligand-binding protein of the invention can also be characterized as a ligand-binding protein having at least 10%, more preferably at least 12%, still more preferably at least 15% and most preferably at least 20% amino acid sequence identity to a vertebrate ligand-gated ion channel but missing any trans-membrane domain. A ligand-gated receptor of the present invention is characterized by having substantially the same ligand-binding characteristics of a vertebrate, preferably mammalian, most preferably human ligand-gated ion channel but comprising at least one alteration in the original amino acid sequence, said

20

25

30

35

WO 01/58951 PCT/EP01/01457

-5

alteration resulting in the presence of an amino acid determining or contributing to the water-solubility of the water-soluble ligand-protein found in molluscs, in particular snails such as those described in more detail below.

The terms "ligand-binding protein", "ligand-binding domain" and "ligand-binding receptor" are meant to at least include the portion of a water-soluble ligand-binding protein or corresponding modified ligand-gated ion channel required for binding a ligand. Minimally the ligand-binding domain consists of a peptide containing that domain. However the use of this term is meant to include a ligand-binding domain or protein that is comprised by a larger portion of, for example, ligand-gated ion channel, such as a fully reconstituted nicotinic acetylcholine receptor.

As shown in Figure 3 the nicotinic acetylcholine receptor (nAChR) belongs to a well-understood member of the ligand-gated ion channels superfamily. The members of this signaling protein group, including 5-HT3, glycine, GABA_A, and GABA_C receptors, are thought to share common secondary, tertiary, and quaternary structures on the basis of a high degree of sequence similarity. Therefore, it is expected that the novel findings in respect to the exemplified AChBP equally apply to the other members of the mentioned ligand-gated ion channels superfamily. Thus, either water-soluble protein being capable of binding a ligand of any of those ligand-gated ion channels may be found in molluscs or the present 5-HT3, GABA_A, and glycine receptors can be modified such as to substantially retain their binding affinity.

Accordingly, the ligand of the water-soluble ligand-binding protein is preferably acetylcholine, gamma-amino-butyric acid (GABA), glycine, nicotine or serotonin. Isolation of such water-soluble ligand-binding proteins can be done as described in Example 1 for the AChBP of the present invention. Instead of α -bungarotoxin other known ligands or can be used for affinity purification. Most preferably, water-soluble ligand-binding protein of the invention is a acetylcholine-binding protein (AChBP). Preferably, the ligand-binding protein displays substantially the binding characteristics shown in Table 2.

The acetylcholine-binding proteins to be used according to the invention are originally derived from aquatic molluscan species, especially species from the class of the snails (Gastropoda), in particular from the order of the lunged snails (Pulmonata). The order of the Pulmonata is divided into the suborders of the Basommatophora (mostly aquatic snails), Systellommatophora and Stylommatophora (mostly land snails). The Basommatophora include the families of the Acroloxidae (e.g. genus Acroloxus), Lymnaeidae (e.g. genera Galba, Stagnicola, Radix and Lymnaea),

10

15

25

30

35

WO 01/58951 PCT/EP01/01457

Physidae (e.g. genera Physa and Aplexa) and Planorbidae (e.g. genera Planorbis, Anisus, Ancylus, Gyraulus, Biomphalaria and Bulinus). Examples of suitable species are *Lymnaea stagnalis* (pond snail) and *Bulinus truncatus*. The isolation of the AChBPs from these snails, cloning of the cDNA encoding these AChBPs and their characterization including the full amino acid sequences is described in the examples. The cDNA and amino acid sequences of the AChBPs of *Lymnaea stagnalis* are depicted in SEQ ID Nos. 1 and 2 (L-AChBP_T1) and SEQ ID Nos. 3 and 4 (L-AChBP_T2). Those of *Bulinus truncatus* are depicted in SEQ ID Nos. 5 and 6 (B-AChBP_T1) and SEQ ID Nos. 7 and 8 (B-AChBP_T2). Features of these proteins are further described in the examples and the accompanying figures.

While a water-soluble ligand-binding protein derived form a Pulmonata species, preferably from a Basommatophora species is preferred, it will be appreciated that the present invention generally relates to any water-soluble protein being capable of binding a ligand of a ligand-gated receptor comprising an amino acid sequence selected from the group consisting of:

- (a) an amino acid sequence as depicted in any one of SEQ ID Nos. 2, 4,
 6 or 8 or a functional equivalent thereof, or a fragment of at least 5 continuous amino acids thereof;
- 20 (b) an amino acid sequence having at least 30% amino acid identity to the amino acid sequence of any one of SEQ ID Nos. 2, 4, 6 or 8; and
 - (c) an amino acid sequence resulting in a protein which is detectable by a monoclonal or polyclonal antibody which recognises, preferably with a binding affinity of at least 10⁻⁷M, a protein comprising an amino acid sequence of (a) or (b).

Identity or similarity, as known in the art, are relationships between two or more polypeptide sequences or two or more polypucleotide sequences, as determined by comparing the sequences. In the art, identity also means the degree of sequence relatedness between polypeptide or polypucleotide sequences, as the case may be, as determined by the match between strings of such sequences. Both identity and similarity can be readily calculated (Computational Molecular Biology, Lesk, ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part I, Griffin and Griffin, eds., Humana Press, New Jersey, 1994; Sequence Analysis in Molecular Biology, von Heinje, Academic Press, 1987; and Sequence Analysis Primer, Gribskov and Devereux, eds., M Stockton Press, New

WO 01/58951 PCT/EP01/01457

-7

York, 1991). While there exist a number of methods to measure identity and similarity between two polynucleotide or two polypeptide sequences, both terms are well known to skilled artisans (von Heinje, supra; Gribskov and Devereux, supra; and Carillo and Lipman SIAM J. Applied Math. 48 (1988), 1073). Methods commonly employed to determine identity or similarity between sequences include, but are not limited to those disclosed in Carillo and Lipman; see supra. Preferred methods to determine identity are designed to give the largest match between the sequences tested. Methods to determine identity and similarity are codified in computer programs. Preferred computer program methods to determine identity and similarity between two sequences include, but are not limited to, GCG program package (Devereux et al., Nucleic Acids Research 12 (1984), 387), BLASTP, BLASTN, psi BLAST and FASTA (Atschul et al., J. Molec. Biol. 215 (1990), 403).

In another embodiment, the present invention relates to a water-soluble protein being capable of binding a ligand of a ligand-gated receptor comprising

- (a) at least the amino acids of the water-soluble protein described above determining solubility of said protein, in the same or corresponding positions as in said protein; and
- (b) at least 4 amino acids determining binding to said ligand.

20

25

30

35

5

10

15

Protein expression studies have shown that wild-type AChBP of the mollusc Lymnaea stagnalis can be produced in Pichia pastoris yeast. The yeast cells express AChBP in a homopentameric form and secrete the protein complex into the medium. The large amounts of AChBP per volume of medium produced (up to 2 mg per liter medium) and the large volumes of yeast that can be cultured allow a large-scale production of AChBP. Besides the wild-type AChBP, various AChBP mutants have been produced in Pichia pastoris. These include mutants containing the following single point mutations (the numbers refer to the amino acid position in the AChBP sequence of Lymnaea stagnalis depicted in SEQ ID No. 2 counted from the first amino acid of the signal peptide; the letter before the number indicates the original amino acid and the letter after the number indicates the mutant amino acid) N85D, H164Y, D194N, Y204P, Y211P and D213N.

Thus the invention pertains to water-soluble proteins derived from molluscan, preferably acetylcholine binding proteins (AChBP's), which are capable of forming multimers, and are capable of binding a ligand of a ligand-gated receptor. These proteins comprise, on the one hand, at least of the amino acids of the AChBP determining solubility of the AChBP in the same positions as in the AChBP, and, on

WO 01/58951 PCT/EP01/01457

-8

the other hand, amino acids determining binding to the ligand of the ligand-gated receptor. The degree of identity with the molluscan AChBP sequence can be defined by amino acid identity, of at least 15%, preferably 20%, more preferably 30%, still more preferably 40%, preferably at least 50 or even at least 60%, preferably more than 70%, more preferably more than 80% and most preferably at least 90% identity, or more, as determined, e.g., using the art-known BLAST algorithm. The amino acids determining binding to the ligand should comprise at least 4 amino acids, preferably at least 6 or even at least 8 amino acids, including a series of at least 3 or 4 amino acids, corresponding to the receptor sequence and preferably differing from the corresponding AChBP amino acids. Preferred embodiments of these proteins are further defined below. Usually, the water-soluble ligand-binding protein or domain as part of a for example chimeric ligand-gated ion channel will comprise 200-240 amino acids. The ligand is preferably acetylcholine, nicotine, lophotoxin, d-tubocurarine, carbamylcholine, galanthamine or epibatidine.

Said ligand-gated receptor can be derived from an arthropod (preferably insect), a plant (preferably a higher plant, most preferably a seed plant) or a chordate (preferably a mammalian, most preferably human), preferably said ligand-gated receptor is a nicotinic acetylcholine receptor.

Usually, the said amino acids in the water-soluble ligand-binding proteins of the invention, which determine solubility are in the same positions as in the AChBP having the amino acid sequence as depicted in any one of SEQ ID Nos. 2, 4, 6 or 8. The solubility determining regions are based on solvent accessibility in structure. The respective amino acid residues can be chosen for example according to Figure 10 or 11 in which the solvent accessible regions are indicated. Preferably, the water-soluble ligand-binding protein of the invention comprises an amino acid sequence having at least 40% amino acid identity to the amino acid sequence of the mature AChBP comprising the amino acid sequence of any one of SEQ ID Nos. 2, 4, 6 or 8, in which the ligand binding amino acids have been replaced with the corresponding amino acids of a ligand-gated receptor.

In one embodiment of the protein of the invention said solubility-determining amino acids (a) comprise hydrophilic amino acids (Asp, Glu, Arg, Lys) from the sequences 20-44, 73-81, 86-92, 112-120, 135-152, 166-189, 196-20, 209-213, and/or 219-227 of SEQ ID No. 2.

The amino acid sequences of L-AChBP_T1 (SEQ ID No. 2) and T2 (SEQ ID No. 4) are almost similar. For the sake of clarity, reference is always made to L-AChBP_T1 (SEQ ID No. 2). However, all references to amino acid residues within are valid for

-9

both T1 and T2, with the noticeable exceptions of Arg(167) becoming Gly(167) and and Thr(203) becoming Ile(203). Furthermore, regarding the amino acid residues (domains) from L-AChBP_T1 and the corresponding residues from B-AChBP the following list provide those amino acid positions in which L-AChBP and B-AChBP differ. All amino acid residue numbers below correspond to their position within the amino acid sequence of the immature protein (numbering starting at methionine (1). One could also start numbering at the start of the amino acid sequence of the mature sequence (L(1)DRAD for L-AChBP and Q(1)IRW for B-AChBP). When using this second method (1st amino acid of the mature seq. = position 1) simply subtract 19 from the L-AChBP position numbers and 21 from the B-AChBP position numbers, for example Asp(36) becomes Asp(17) for L-AChBP) and Asp(15) for B-AChBP. For the further embodiments the positions are given for L-AChBP T1 (SEQ ID No. 2) followed by an indication of the corresponding amino acid positions in the amino acid sequence of L-AChBP_T2 (SEQ ID No. 4) and B-AChBP_T1 (SEQ ID No. 6) & B-AChBP_T2 (SEQ ID No. 8) in the form of (L-AChBP_T1&T2: B-AChBP_T1&T2).

In a preferred embodiment said solubility determining amino acids (a) comprise amino acids Asp(36), Asp(68), Glu(115), Arg(137), Asp(143), Asp(148), Glu(150), Arg(167), Arg(189), Glu(215) of SEQ ID No.2, wherein Asp may be exchanged for Glu and vice versa and Lys may be exchanged for Arg and vice versa (L-AChBP_T1&T2: B-AChBP_T1&T2; Asp(36): Asp(36); Asp(68): Asp(68); Glu(115): Glu(116); Arg(137): Arg(138); Asp(143): Asp(144); Asp(148): Asp(149); Glu(150): Glu(151); Arg(167): Gly(167), in L-AChBP_T2: Lys(168); Arg(189): Lys(190); Glu(215): Glu(216).

25

30

35

10

15

20

In a still more preferred embodiment the water-soluble ligand-binding protein comprises the amino acids Cys(142), Thr(149), Ala(153), Thr(154), Cys(155), Arg(156), Ile(157) and/or Lys(158) of SEQ ID No. 2. (L-AChBP_T1&T2: B-AChBP_T1&T2; Cys(142): Cys(143); Thr(149): Thr(150); Ala(153): Ala(154); Thr(154): Thr(155); Cys(155): Cys(156); Arg(156): Arg(157); Ile(157): Ile(158); Lys(158): Lys(159). In a further embodiment the water-soluble ligand-binding protein comprises either in addition or alternatively the amino acids (b) Pro(39), Trp(77), Trp(101), Pro(103), Asp(194), and/or Ser(161) of SEQ ID No. 2 (L-AChBP_T1&T2: B-AChBP_T1&T2; Pro(39): Pro(39); Trp(77): Trp(77); Trp(101): Trp(102); Pro(103): Pro(104); Ser(161): Ser(162); Asp(194): Ser(195).

In a still further embodiment the water-soluble ligand-binding protein comprises either

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-10

in addition or alternatively to the above described embodiments amino acid sequences 165-169 and/or 200-203 of SEQ ID No. 2 have been exchanged with the corresponding sequence of the ligand-gated receptor (L-AChBP_T1&T2: B-AChBP_T1&T2; His(165)-Iso(169):. Asp(166)-Phe(170) (B-AChBP_T1): Asp(166)-Leu(170) (B-AChBP_T2); Asn(200)-Thr(203); Iso(203) for L-AChBP_T2: Asn(201)-Lys(204).

The amino acids determining binding to the ligand of the nicotinic acetylcholine receptor include three stretches on the nAChR alpha subunits. These stretches contain amino acids that are conserved throughout the various nAChR alpha subunits and that are essential for ligand binding. These stretches (corresponding to the Torpedo alpha subunit) are (numbering of nAChR α7 as depicted in SEQ ID No. 9): Trp (108) - Tyr (115), Trp (108) and Tyr (115) being essential; Trp (171) - Tyr (173), the amino acids Trp (171) and Tyr (173) being essential; Tyr (210) - Tyr (217), the amino acids Tyr (210), Cys (212), Cys (213) and Tyr (217) being essential. In the chimeric proteins according to the invention, at least the essential amino acids of at least one of these stretches haven been substituted for the corresponding amino acids. Preferably, the entire stretches have been substituted.

In a particularly preferred embodiment of the invention, the water-soluble ligand-binding protein is capable of binding a ligand of an acetylcholine receptor, wherein in said protein at least one of the amino acid sequences Trp(101) - Tyr(T108), Trp(162) - His(164) and Tyr(204) - Tyr(211) of SEQ ID No. 2 has been exchanged with the corresponding sequence of the acetylcholine receptor (L-AChBP_T1&T2: B-AChBP_T1&T2; Trp(101)-Tyr(108): Trp(102)-Tyr(109); Trp(162)-His(164): Trp(163)-His(165), (B-AChBP_T1): Trp(163)-Phe(165) (B-AChBP_T2); Tyr(204)-Tyr(211): Tyr(205)-Tyr(212).

On the basis of homology to the AChBPs, it is possible to change amino acid residues in the original amino acid sequence of the ligand-gated ion channel, which are not critical to ligand-binding or essential for the tertiary and quaternary structure of the receptor but could be substituted to amino acid residues which according to the AChBP in particular the crystal structure contributes to their water-solubility. As a result the ligand-gated ion channel or its ligand-binding domain or the respective monomers and pentamers are for example expected to be more easily expressible in recombinant expression system and more importantly amenable to crystallization, allowing the construction of three-dimensional models of their ligand binding domains.

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-11

Thus, in another embodiment the present invention relates to a method for the production of a water-soluble ligand-gated receptor or a corresponding ligand-binding domain or for improving the water solubility and accessibility to crystallization of such a receptor or domain, said method comprising altering the amino acid sequence of the extracellular domain of a ligand-gated receptor by way of substituting, adding, deleting or modifying at least one amino acid at a position corresponding to an amino acid determining or contributing to the water-solubility of the above-described watersoluble ligand-binding protein of the present invention The method of the invention can be performed using conventional techniques known in the art, for example, by using amino acid deletion(s), insertion(s), substitution(s), addition(s), and/or recombination(s) and/or any other modification(s) known in the art either alone or in combination. Methods for introducing such modifications in the DNA sequence underlying the amino acid sequence of the ligand-binding domain a ligand-gated ion channel are well known to the person skilled in the art; see, e.g., Sambrook, Molecular Cloning A Laboratory Manual, Cold Spring Harbor Laboratory (1989) N.Y. The resulting ligand-gated receptor or ligand-binding domain retains comparable in vitro and preferably also in vivo ligand-binding activity to that of the ligand-gated ion channel, and more importantly, allow complete crystallization of the protein such that they may be characterized by X-ray crystallography. The X-ray crystallographic data can be used for example for identification and construction of possible therapeutic compounds in the treatment of various disease conditions.

As has been discussed herein before, the ligand-gated ion channel superfamily including nACh, 5-HT3, glycine, GABA_A, and GABA_C receptors as well as invertebrate glutamate ion-channels and MOD-1 serotonin channel contain extracellular ligand binding domains that are homologous to the AChBP. Many of these receptors are promising drug targets. Therefore, the ligand-gated receptor to be modified is preferably one of those of the mentioned superfamily, most preferably it is nAChR.

Information on the nucleotide and amino acid sequences, structural elements, functional assays of the nAch, 5-HT3, glycine, GABA_A, and GABA_C receptors can be found in the prior art. For example, the nicotinic receptors at the amino acid level are described in Corringer et al., Annu. Rev. Pharmacol. Toxicol. 40 (2000), 431-458. Means for retrieving nucleotide and amino acid sequences, performing sequence alignments in order to identify the most likely critical amino acid residues are described below and in the examples; for further general information see the review on periplasmic binding protein (PBP), an ancient protein module present in multiple drug receptors by Felder et al., PharmSci. 1(2) (1999).

į.

5

10

15

20

25

35

In a preferred embodiment of the method of the present invention, said at least one amino acid is altered to the corresponding amino acid of the amino acid sequence depicted in any one of SEQ ID Nos. 2, 4, 6 or 8, or to a an equivalent amino acid, preferably in which said solubility-determining amino acids comprise solvent accessible regions in the crystal structure according to Figure 10 or 11. Preferred amino acid sequence positions and amino acid substitutions are described above for the AChBP and can be applied generally in the method of the present invention.

It is expected that the insertion of the loop Cys123-Cys136 of the mature AChBP SEQ ID No. 2 into the equivalent region (Cys127-Cys141) in the mature nicotinic α 7 homopentamer ligand binding domain creates an easily expressed form of this protein. Likewise, this loop or an equivalent loop from other water-soluble ligand proteins of the present invention can be inserted into the equivalent region of other homopentameric ligand binding domains of ligand gated ion channels such as the glycine receptor and the 5-HT3 receptor to create an easily expressed form of those proteins.

Thus, in one embodiment, the present invention relates to any one of the above described methods, wherein loop Cys123-Cys136 of SEQ ID No. 2 is inserted into the corresponding region of the ligand binding domain of the ligand-gated receptor.

The above described water-soluble ligand-gated receptor or a corresponding ligand-binding domain are usually prepared by site-directed mutagenesis of the underlying encoding polynucleotide. Once the corresponding polynucleotide has been generated it can be used to express the altered ligand-gated receptor or a corresponding ligand-binding domain. Thus, the method of the present invention commonly comprises

- (a) culturing a host cell transfected with and capable of expressing a polynucleotide comprising a nucleotide sequence encoding the altered amino acid sequence; and optionally
- 30 (b) recovering said water-soluble ligand-gated receptor or corresponding ligand-binding domain from the culture.

Methods for the expression and purification of the water-soluble ligand-gated receptor or corresponding ligand-binding domain of the present invention are described further below. Preferably, the expression system described in Examples 4 and 5, or corresponding expression systems are used.

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-13

The present invention also relates to the a water-soluble ligand-gated receptor and ligand-binding domain obtainable by the above described methods of the invention. Preferably, said water-soluble ligand-gated receptor exhibits a 10-fold, more preferably 100-fold, still more preferably 1000-fold and most preferably 10000-fold higher solubility in water than the corresponding wild type, preferably human ligand-gated receptor. However, improvements in water solubility of about 2 to 5 fold is also already advantageous. The average hydrophobicity may be in the range of –100 to –400. Accordingly, the present invention provides methods for the prediction and creation of mutants and chimeras of ligand binding domains of homopentameric acetylcholine receptor subtypes and of other homopentameric ion channels with increased solubility.

In one embodiment the water-soluble ligand-binding protein of the invention further comprises a spacer sequence allowing coupling with a carrier body. The spacer sequence may be an amino acid sequence encodable by a polynucleotide or other molecule such as polymethylene anchor groups commonly used in chip technology. The chimeric protein of the invention may further comprise a spacer sequence, which allows coupling of the protein to a carrier body. Such spacer sequence may be e.g. an oligo-histidine stretch attached to the C-terminus of the protein. Such an oligohistidine stretch is capable of binding to Talon@ metal affinity beads or similar carriers. Such binding stretches have no detectable influence on the pharmacological properties of the proteins. The chimeric proteins according to the invention can be used for screening of specific binding of potential drugs, in particular screening for modulators of jon-channel opening. Conventional in vitro screening techniques, such as phage display technology, can be used for this purpose. High-throughput assays, possibly in combination with combinatorial chemistry can also be used. Specific binding of test compounds to the (immobilised) chimeric proteins of the invention can be performed e.g. by competition binding assays using alpha bungarotoxin as a competitor. The invention also concerns test kits containing the proteins described above, together with further means for carrying out a screening test, such as carriers, labels, diluents, other chemicals etc.

In addition, the present invention relates to fusion proteins comprising the watersoluble ligand-binding protein of the invention or a binding fragment thereof and a fragment of a ligand-gated receptor. The term "fusion protein" as used herein refers to protein constructs that are the result of combining multiple protein domains or linker regions for the purpose of gaining the combined functions of the domains or

10

15

20

25

WO 01/58951 PCT/EP01/01457

-14

linker regions. This is may be accomplished by molecular cloning of the nucleotide sequences encoding such domains to produce a new polynucleotide sequence that encodes the desired fusion protein. Alternatively, creation of a fusion protein may be accomplished by chemically joining two proteins. A fusion protein of the present invention preferably comprises at least the ligand-binding domain of the AChBP or of a ligand-gated ion channel, which has been modified in accordance with the above described methods.

Nicotinic acetylcholine receptors are comprised of five subunits, selected from a related family of subunit proteins. The neuronal subunits fall into two main types depending on the presence or absence of a pair of vicinal cysteines close to the binding site for acetylcholine. Thus all α -subunits contain paired cysteine residues thought to play a role in binding of nicotinic agonists (Aplin and Wonnacott, 48 (1994), 473-477), whereas the β -subunits do not. There are ten known alpha subunits, $\alpha 1$ to α 10, and at least four beta subunits, β 1 to β 4. Receptors comprise at least one alpha subunit which in some cell types combine with a beta subunit and in some cases a gamma, delta and epsilon subunit. For example, the AChR at the neuromuscular junction is believed to have an $(\alpha 1)2\beta 1\gamma\delta$ stoichiometry. Within the group of α subunits there is marked diversity in the manner in which a complete functional nAChR is formed. The majority of the α subunits only form functional receptors when combined as a heteropentamer with β -subunits in the CNS (McGehee and Role, Annual Review of Physiology 57 (1995), 521-546). However, α 7, α 8 and α 9 nAChR subunits and the related 5-HT3A subunit are capable of forming functional homopentameric receptors. In this respect it is interesting that the phylogenetic relationship between nAChR subunits suggest that α7, α8, α9 and the related 5-HT3A subunit are more related to each other than to the subunits which only form heteropentameric receptors. Sequence homologies indicate that the α 7, α 8 and α 9 subunits form a distinct subgroup of the alpha subunits.

As is evident form the foregoing, the above described water-soluble ligand-binding protein or receptor or ligand-binding domain thereof can be used for forming complexes of homo- or heteromultimers, such as a dimer, pentamer or decamer consisting of at least one monomer of the mentioned proteins of the present invention. Preferably, these multimers constitute a function ligand-gated receptor. Preferably, said ligand-gated receptor is related to the nAchR.

35

30

The present invention also relates to the production of synthetic heteropentamers resembling heteropentameric gated ion-channels by mutation of AChBP, using

۲,

WO 01/58951 PCT/EP01/01457

-15

knowledge of the crystal structure about the primary and secondary contact regions; see infra. Preferably, said synthetic heteropentamer's resembles a heteropentameric nicotinic acetylcholine receptor. Accordingly, the present invention more generally relates to a ligand-gated ion channel comprising any one of the above described water-soluble ligand-binding proteins or receptors of the invention as a monomer, homo- or heterodimer or -pentamer. This method therefore allows the prediction and creation of mutants and chimeras of nicotinic acetylcholine receptors and other ligand-gated ion channels that are insensitive or more sensitive to toxin binding, e.g. bungarotoxin, lophotoxin, conotoxin, and other toxins that inhibit ligand-gated ion channels. Preferably, said ligand-gated ion channel is less or more sensitive to binding of toxins such as bungarotoxin, lophotoxin or conotoxin compared to the wild type ligand-gated ion channel.

Further information and examples how to create chimeric ligand-binding proteins in accordance with the present invention is given in Example 10.

15

20

25

30

35

10

The nucleotide and amino acid sequences of the acetylcholine, 5-HT3, glycine, GABA_A, and GABA_C receptors can be easily retrieved from public database, for example from the internet using http://www.ncbi.nlm.nih.gov/Entrez. The citations also include a reference to the corresponding publication also reporting on the functional expression of the respective receptor.

The use of recombinant acetylcholine-gated ion channels and functionally assays in the discovery of putative novel ligands has been described in Cosford, Pharm. Acta Helv. (2000), 74(2-3), 125-130. Furthermore, the cell-free expression and functional reconstitution of homo-oligomeric α7 nicotinic acetylcholine receptors into planar lipid bilayers has been reported by Lyford and Rosenberg, J. Biol. Chem. (1999), 274(36), 25675-25681. The use of functional assays of cloned and native muscarinic acetylcholine receptors for determining the selectivity profile of toxins has been described by Olianas et al. (J. Pharmacol. Exp. Ther. 288 (1999), 164-170). A system for the evaluation of pharmacological differences and similarities between 5-HT3 receptors stably transfected cells is provided by for example Bruss et al., Naunyn-Schmiedebergs Archives of Pharmacology 360 (1999), 225-33. The primary structure and functional expression of the 5-HT3 receptor is described in Maricq et al., Science 254 (1991), 432-437. Likewise, the stable expression of human glycine $\alpha 1$ and $\alpha 2$ receptor monomers in mouse L(tk-) cells and their use for the study of the physiology and pharmacology of functional glycine receptors is described in Wick et al., J. Neurosci. Methods 87 (1999), 97-103. An example for the measurement of the WO 01/58951 PCT/EP01/01457

-16

pharmacology of recombinant GABA_A receptor subtypes is described in Simpson et al., J. Neurosci. Methods 99 (2000), 91-100. Further examples for assay systems are given below.

The described methods as well as others known to the person skilled in the art can be used for example to

- (1) express and characterise the water-soluble ligand-binding proteins and ligand-gated ion channels of the present invention; and
- (2) use stably transfected cells expressing the above described ligand-gated ion channels for the identification of novel ligands.

10

15

20

25

30

35

The present invention also relates to polynucleotides encoding the water-soluble ligand-binding proteins and ligand-gated ion channels of the present invention, and multimers thereof, preferably dimers or pentamers. Such polynucleotide may be a DNA such as a cDNA, or an RNA such as mRNA or any other form of nucleic acid including synthetic or modified derivatives and may encode the polypeptide in a continuous sequence or in a number of sequences interrupted by intervening sequences. In which ever form it is present, the polynucleotide is an isolated polynucleotide in that it is removed from its naturally-occurring state. This aspect of the invention is based on the cloning of the cDNA for ligand-binding proteins. In a preferred embodiment, the polynucleotide comprises the nucleotide sequence of any one of SEQ ID Nos. 1, 3, 5 or 7, optionally including one or more mutations or deletions which do not substantially affect the activity of the polypeptide encoded thereby. Such mutations include those arising from the degeneracy of the genetic code, as well as those giving rise to any of the amino acid mutations or deletions discussed above. The polynucleotides of the invention preferably comprise

- (a) a nucleotide sequence having at least 15 continuous nucleotides of the nucleotide sequence depicted in any one of SEQ ID Nos. 1, 3, 5 or 7 or a degenerated nucleotide sequence thereof; or
- (b) a nucleotide sequence capable of hybridizing to a nucleotide sequence of (a) under stringent hybridisation conditions.

Typically, selective hybridization will occur when there is at least about 55% sequence identity -- preferably at least about 65%, more preferably at least about 75%, and most preferably at least about 90% -- over a stretch of at least about 14 nucleotides; see, e.g., Kanehisa, Nucleic Acids Res. 12 (1984), 203-213, herein incorporated by reference. Nucleic acid hybridization will be affected by such conditions as salt concentration, temperature, solvents, the base composition of the

15

25

30

35

WO 01/58951 PCT/EP01/01457

-17

hybridizing species, length of the complementary regions, and the number of nucleotide base mismatches between the hybridizing nucleic acids, as will be readily appreciated by those skilled in the art.

"Stringent hybridization conditions" and "stringent wash conditions" in the context of nucleic acid hybridization experiments depend upon a number of different physical parameters. The most important parameters include temperature of hybridization, base composition of the nucleic acids, salt concentration and length of the nucleic acid. One having ordinary skill in the art knows how to vary these parameters to achieve a particular stringency of hybridization. In general, "stringent hybridization" is performed at about 25°C below the thermal melting point (T m) for the specific DNA hybrid under a particular set of conditions.

"Stringent washing" is performed at temperatures about 5°C lower than the Tm for the specific DNA hybrid under a particular set of conditions. The Tm is the temperature at which 50% of the target sequence hybridizes to a perfectly matched probe; see Sambrook et al., page 9.51, hereby incorporated by reference. The Tm for a particular DNA-DNA hybrid can be estimated by the formula:

Tm = 81.5°C + 16.6 (log10[Na+]) + 0.41 (fraction G + C) - 0.63 (% formamide) - (600/l) where I is the length of the hybrid in base pairs.

The Tm for a particular RNA-RNA hybrid can be estimated by the formula:

20 Tm = 79.8° C + 18.5 (log10[Na+]) + 0.58 (fraction G + C) + 11.8 (fraction G + C)2 - 0.35 (% formamide) - (820/1).

The Tm for a particular RNA-DNA hybrid can be estimated by the formula: $Tm = 79.8^{\circ}C + 18.5(log10[Na+]) + 0.58$ (fraction G + C) + 11.8 (fraction G + C)2 - 0.50 (% formamide) - (820/l).

In general, the Tm decreases by 1-1.5°C for each 1% of mismatch between two nucleic acid sequences. Thus, one having ordinary skill in the art can alter hybridization and/or washing conditions to obtain sequences that have higher or lower degrees of sequence identity to the target nucleic acid. For instance, to obtain hybridizing nucleic acids that contain up to 10% mismatch from the target nucleic acid sequence, 10-15°C would be subtracted from the calculated Tm of a perfectly matched hybrid, and then the hybridization and washing temperatures adjusted accordingly. Probe sequences may also hybridize specifically to duplex DNA under certain conditions to form triplex or other higher order DNA complexes. The preparation of such probes and suitable hybridization conditions are well known in the art. An example of stringent hybridization conditions for hybridization of complementary nucleic acid sequences having more than 100 complementary residues on a filter in a Southern or Northern blot or for screening a library is 50%

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-18

formamide/6X SSC at 42°C for at least ten hours. Another example of stringent hybridization conditions is 6X SSC at 68°C for at least ten hours. An example of low stringency hybridization conditions for hybridization of complementary nucleic acid sequences having more than 100 complementary residues on a filter in a Southern or northern blot or for screening a library is 6X SSC at 42°C for at least ten hours. Hybridization conditions to identify nucleic acid sequences that are similar but not identical can be identified by experimentally changing the hybridization temperature from 68°C to 42°C while keeping the salt concentration constant (6X SSC), or keeping the hybridization temperature and salt concentration constant (e.g. 42°C and 6X SSC) and varying the formamide concentration from 50% to 0%. Hybridization buffers may also include blocking agents to lower background. These agents are well-known in the art; see Sambrook et al., pages 8.46 and 9.46-9.58, herein incorporated by reference. Wash conditions also can be altered to change stringency conditions. An example of stringent wash conditions is a 0.2x SSC wash at 65°C for 15 minutes (see Sambrook et al., for SSC buffer). Often the high stringency wash is preceded by a low stringency wash to remove excess probe. An exemplary medium stringency wash for duplex DNA of more than 100 base pairs is 1x SSC at 45°C for 15 minutes. An exemplary low stringency wash for such a duplex is 4x SSC at 40°C for 15 minutes. In general, signal-to-noise ratio of 2x or higher than that observed for an unrelated probe in the particular hybridization assay indicates detection of a specific hybridization.

By the provision of the nucleotide sequences of SEQ ID Nos. 1, 3, 5 and 7 as well as those encoding the amino acid sequences depicted in SEQ ID Nos. 2, 4, 6 and 8 it is possible to isolate identical or similar nucleic acid molecules which encode water-soluble ligand-binding proteins from other species or organisms, in particular orthologous water-soluble ligand-binding protein encoding genes from mammals. The term "orthologous" as used herein means homologous sequences in different species that arose from a common ancestor gene during speciation. Orthologous genes may or may not be responsible for a similar function; see, e.g., the glossary of the "Trends Guide to Bioinformatics", Trends Supplement 1998, Elsevier Science.

In a further aspect, the present invention provides a recombinant polynucleotide comprising a vector incorporating the polynucleotide of the present invention. Many suitable vectors are known to those skilled in molecular biology, the choice of which would depend on the function desired and include plasmids, cosmids, viruses, bacterlophages and other vectors used conventionally in genetic engineering. Methods which are well known to those skilled in the art can be used to construct

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-19

various plasmids and vectors; see, for example, the techniques described in Sambrook, Molecular Cloning A Laboratory Manual, Cold Spring Harbor Laboratory (1989) N.Y. and Ausubel, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. (1989), (1994). Alternatively, the polynucleotides and vectors of the invention can be reconstituted into liposomes for delivery to target cells. As discussed in further details below, a cloning vector was used to isolate individual sequences of DNA. Relevant sequences can be transferred into expression vectors where expression of a particular polypeptide is required. Typical cloning vectors include pBscpt sk, pGEM, pUC9, pBR322 and pGBT9. Typical expression vectors include pTRE, pCAL-n-EK, pESP-1, pOP13CAT, pET, pGEX, pMALC, pPIC9, pBac.

Hence, in a preferred embodiment of the present invention the above-described polyncucleotides either alone or present in a vector are linked to control sequences which allow the expression of the polynucleotide in prokaryotic and/or eukaryotic cells.

The term "control sequence" refers to regulatory DNA sequences which are necessary to effect the expression of coding sequences to which they are ligated. The nature of such control sequences differs depending upon the host organism. In prokaryotes, control sequences generally include promotor, ribosomal binding site, and terminators. In eukaryotes generally control sequences include promotors, terminators and, in some instances, enhancers, transactivators or transcription factors. The term "control sequence" is intended to include, at a minimum, all components the presence of which are necessary for expression, and may also include additional advantageous components.

The term "operably linked" refers to a juxtaposition wherein the components so described are in a relationship permitting them to function in their intended manner. A control sequence "operably linked" to a coding sequence is ligated in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequences. In case the control sequence is a promotor, it is obvious for a skilled person that double-stranded nucleic acid is preferably used.

Thus, the vector of the invention is preferably an expression vector. An "expression vector" is a construct that can be used to transform a selected host cell and provides for expression of a coding sequence in the selected host. Expression vectors can for instance be cloning vectors, binary vectors or integrating vectors. Expression comprises transcription of the nucleic acid molecule preferably into a translatable mRNA. Regulatory elements ensuring expression in prokaryotic and/or eukaryotic

15

20

25

30

35

-20

cells are well known to those skilled in the art. In the case of eukaryotic cells they comprise normally promotors ensuring initiation of transcription and optionally poly-A signals ensuring termination of transcription and stabilization of the transcript. Possible regulatory elements permitting expression in prokaryotic host cells comprise, e.g., the PL, lac, trp, T7 or tac promotor in E. coli, and examples of regulatory elements permitting expression in eukaryotic host cells are the AOX1 or GAL1 promotor in yeast or the CMV-, SV40-, RSV-promotor (Rous sarcoma virus), CMV-enhancer, SV40-enhancer or a globin intron in mammalian and other animal cells. In this context, suitable expression vectors are known in the art such as Okayama-Berg cDNA expression vector pcDV1 (Pharmacia), pCDM8, pRc/CMV, pcDNA1, pcDNA3 (In-vitrogene), pSPORT1 (GIBCO BRL). An alternative expression system which could be used to express the protein is an insect system. In one such system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in Spodoptera frugiperda cells or in Trichoplusia larvae. The coding sequence of a nucleic acid molecule of the invention may be cloned into a nonessential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promotor. Successful insertion of said coding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein coat. The recombinant viruses are then used to infect S. frugiperda cells or Trichoplusia larvae in which the protein of the invention is expressed (Smith, J. Virol. 46 (1983), 584; Engelhard, Proc. Nat. Acad. Sci. USA 91 (1994), 3224-3227).

In plants, promotors commonly used are the polyubiquitin promotor, and the actin promotor for ubiquitous expression. The termination signals usually employed are from the Nopaline Synthase promotor or from the CAMV 35S promotor. A plant translational enhancer often used is the TMV omega sequences, the inclusion of an intron (Intron-1 from the Shrunken gene of maize, for example) has been shown to increase expression levels by up to 100-fold. (Mait, Transgenic Research 6 (1997), 143-156; Ni, Plant Journal 7 (1995), 661-676). Additional regulatory elements may include transcriptional as well as translational enhancers. Advantageously, the above-described vectors of the invention comprises a selectable and/or scorable marker. Selectable marker genes useful for the selection of transformed cells and, e.g., plant tissue and plants are well known to those skilled in the art and comprise, for example, antimetabolite resistance as the basis of selection for dhfr, which confers resistance to methotrexate (Reiss, Plant Physiol. (Life Sci. Adv.) 13 (1994), 143-149); npt, which confers resistance to the aminoglycosides neomycin,

. 10

20

25

30

35

WO 01/58951 PCT/EP01/01457

-21

kanamycin and paromycin (Herrera-Estrella, EMBO J. 2 (1983), 987-995) and hygro, which confers resistance to hygromycin (Marsh, Gene 32 (1984), 481-485).

Useful scorable markers are also known to those skilled in the art and are commercially available. Advantageously, said marker is a gene encoding luciferase (Giacomin, Pl. Sci. 116 (1996), 59-72; Scikantha, J. Bact. 178 (1996), 121), green fluorescent protein (Gerdes, FEBS Lett. 389 (1996), 44-47) or ß-glucuronidase (Jefferson, EMBO J. 6 (1987), 3901-3907). This embodiment is particularly useful for simple and rapid screening of cells, tissues and organisms containing a vector of the invention.

The proteins can be recovered and purified from recombinant cell cultures by wellknown methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, size exclusion chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") or FPLC is employed 15 for purification.

The present invention furthermore relates to host cells produced by introducing a nucleic acid molecule into the host cell which upon its presence in the cell mediates the expression of a gene encoding water-soluble ligand-binding proteins or comprising a polynucleotide or a vector as described above or a polynucleotide according to the invention wherein the polynucleotides and/or nucleic acid molecule is foreign to the host cell. By "foreign" it is meant that the polynucleotide or nucleic acid molecule is either heterologous with respect to the host cell, this means derived from a cell or organism with a different genomic background, or is homologous with respect to the host cell but located in a different genomic environment than the naturally occurring counterpart of said nucleic acid molecule. This means that, if the nucleic acid molecule is homologous with respect to the host cell, it is not located in its natural location in the genome of said host cell, in particular it is surrounded by different genes. In this case the polynucleotide may be either under the control of its own promotor or under the control of a heterologous promotor. The vector or nucleic acid molecule according to the invention which is present in the host cell may either be integrated into the genome of the host cell or it may be maintained in some form extrachromosomally. In this respect, it is also to be understood that the nucleic acid molecule of the invention can be used to restore or create a mutant gene via homologous recombination.

10

15

20

25

30

WO 01/58951 PCT/EP01/01457

-22

The host cell can be any prokaryotic or eukaryotic cell, such as bacterial, insect, fungal, plant or animal cells.

The term "prokaryotic" is meant to include all bacteria which can be transformed or transfected with a DNA or RNA molecules for the expression of a protein of the invention. Prokaryotic hosts may include gram negative as well as gram positive bacteria such as, for example, E. coli, S. typhimurium, Serratia marcescens and Bacillus subtilis. The term "eukaryotic" is meant to include yeast, higher plant, insect and preferably mammalian cells. Depending upon the host employed in a recombinant production procedure, the protein encoded by the polynucleotide of the present invention may be glycosylated or may be non-glycosylated. The water-soluble ligand-binding protein of the invention may or may not also include an initial methionine amino acid residue. A polynucleotide of the invention can be used to transform or transfect the host using any of the techniques commonly known to those of ordinary skill in the art. Furthermore, methods for preparing fused, operably linked genes and expressing them in, e.g., mammalian cells and bacteria are well-known in the art (Sambrook, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1989).

Thus the present invention provides a cell capable of expressing a polypeptide as discussed herein. The cell comprises a recombinant host cell usually incorporating the polynucleotide. Preferably, the host cell incorporates the polynucleotide as the recombinant polynucleotide. Any suitable host cell may be chosen, again depending on the intended purpose. Suitable host cells include XLI-BLUE, B21(DE3)pLysS, HB101, SOLR and SP-Q01 (Saccharomyces pombe).

Using an appropriate combination of host cell, vector and polynucleotide, an expression system can be provided so as to obtain a polypeptide useful in the present invention. This may comprise a fusion polypeptide encoded by the recombinant polynucleotide, a part of which is encoded by the vector. Typically, the vector will have a promotor region, which is usually inducible, leading to 5' coding region associated with the promotor. By appropriate manipulation, the polynucleotide encoding the polypeptide can be attached to the 5' coding region in frame. In this way, expression of the nucleotide sequence downstream of the promotor region gives rise to the fusion polypeptide which includes the polypeptide of the present invention.

The present invention also relates to an antigen comprising an epitope of at least 5 continuous amino acids of the amino acid sequence depicted in any one of SEQ ID Nos. 2, 4, 6 or 8 and/or said epitope is detectable by a monoclonal or polyclonal

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-23

antibody which recognises, preferably with a binding affinity of at least 10-7M, a protein of the invention as described above. In the present invention, "epitopes" refers to fragments of the AChBP of the invention having antigenic or immunogenic activity in an animal. A preferred embodiment of the present invention relates to antigens comprising an epitope, as well as the polynucleotide encoding this fragment. A region of a protein molecule to which an antibody can bind is defined as an "antigenic epitope." In contrast, an "immunogenic epitope" is defined as a part of a protein that elicits an antibody response; see, for instance, Geysen, Proc. Natl. Acad. Sci. USA 81 (1983); 3998-4002. Fragments which function as epitopes may be produced by any conventional means; see, e.g., Houghten, Proc. Natl. Acad. Sci. USA 82 (1985), 5131-5135 further described in U.S. Patent No. 4,631,211. In the present invention, antigenic epitopes preferably contain a sequence of at least five, six, seven, more preferably at least nine, and most preferably between about 15 to about 30 amino acids. Antigenic epitopes are useful to raise antibodies, including monoclonal antibodies, that specifically bind the epitope; see, for instance, Wilson, Cell 37 (1984), 767-778; Sutcliffe, Science 219 (1983), 660-666), Similarly, immunogenic epitopes can be used to induce antibodies according to methods well known in the art; see, for instance, Sutcliffe, supra; Wilson, supra; Chow, Proc. Natl. Acad. Sci. USA 82 (1985), 910-914; and Bittle, J. Gen. Virol. 66 (1985); 2347-2354. A preferred immunogenic epitope includes the soluble protein. The immunogenic epitopes may be presented together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse) or, if it is long enough (at least about 25 amino acids), without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting.)

The present invention also relates to antibodies specifically recognizing the water-soluble ligand-binding protein and ligand-gated ion channels of the present invention, in particular recognizing the above described antigen or epitope. As used herein, the term "antibody" (Ab) or "monoclonal antibody" (Mab) is meant to include intact molecules as well as antibody fragments (such as, for example, Fab and F(ab')₂ fragments) which are capable of specifically binding to protein. Fab and F(ab')₂ fragments lack the Fc fragment of intact antibody, clear more rapidly from the circulation, and may have less non-specific tissue binding than an intact antibody; see, e.g., Wahl, J. Nucl. Med. 24 (1983), 316-325. Thus, these fragments are preferred, as well as the products of a FAB or other immunoglobulin expression

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-24

library. Moreover, antibodies of the present invention include chimeric, single chain, and humanized antibodies; see also infra. Said antibody can be a monoclonal antibody, a polyclonal antibody, a single chain antibody, human or humanized antibody, primatized, chimerized or fragment thereof that specifically binds said peptide or polypeptide also including bispecific antibody, synthetic antibody, antibody fragment, such as Fab, Fv or scFv fragments etc., or a chemically modified derivative of any of these. The general methodology for producing antibodies is well-known and has been described in, for example, Köhler and Milstein, Nature 256 (1975), 494 and reviewed in J.G.R. Hurrel, ed., "Monoclonal Hybridoma Antibodies: Techniques and Applications", CRC Press Inc., Boco Raron, FL (1982), as well as that taught by L. T. Mimms et al., Virology 176 (1990), 604-619. Furthermore, antibodies or fragments thereof to the aforementioned peptides can be obtained by using methods which are described, e.g., in Harlow and Lane "Antibodies, A Laboratory Manual", CSH Press, Cold Spring Harbor, 1988. For the production of antibodies in experimental animals, various hosts including goats, rabbits, rats, mice, and others, may be immunized by injection with polypeptides of the present invention or any fragment or oligopeptide or derivative thereof which has immunogenic properties. Techniques for producing and processing polyclonal antibodies are known in the art and are described in, among others, Mayer and Walker, eds., "Immunochemical Methods in Cell and Molecular Biology", Academic Press, London (1987). Polyclonal antibodies also may be obtained from an animal, preferably a mammal, previously infected with the virus of the invention. Methods for purifying antibodies are known in the art and comprise, for example, immunoaffinity chromatography. Depending on the host species, various adjuvants or immunological carriers may be used to increase immunological responses. Such adjuvants include, but are not limited to, Freund's, complete or incomplete adjuvants, mineral gels such as aluminium hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions and dinitrophenol. An example of a carrier, to which, for instance, a peptide of the invention may be coupled, is keyhole limpet hemocyanin (KLH). When derivatives of said antibodies are obtained by the phage display technique, surface plasmon resonance as employed in the BIAcore system can be used to increase the efficiency of phage antibodies which bind to an epitope of the peptide or polypeptide of the invention (Schier, Human Antibodies Hybridomas 7 (1996), 97-105; Malmborg, J. Immunol. Methods 183 (1995), 7-13). In many cases, the binding phenomena of antibodies to antigens is equivalent to other ligand/anti-ligand binding.

15

20

25

30

35

-25

In another embodiment the present invention relates to an oligonucleotide probe comprising a nucleotide sequence having at least 15 continuous nucleotides of a polynucleotide of the invention and/or encoding the above described antigen. Such oligonucleotides will usually specifically hybridize to a polynucleotide encoding a water-soluble ligand-binding protein of the invention. Specific hybridization occurs preferably under stringent conditions and implies no or very little cross-hybridization with nucleotide sequences encoding no or substantially different proteins. Such nucleic acid molecules may be used as probes and/or for the control of gene expression. Nucleic acid probe technology is well known to those skilled in the art who will readily appreciate that such probes may vary in length. Preferred are nucleic acid probes of 17 to 35 nucleotides in length. Of course, it may also be appropriate to use nucleic acids of up to 100 and more nucleotides in length. The nucleic acid probes of the invention are useful for various applications. On the one hand, they may be used as PCR primers for amplification of polynucleotides according to the invention. Another application is the use as a hybridization probe to identify polynucleotides hybridizing to the polynucleotides of the invention by homology screening of genomic DNA libraries. Nucleic acid molecules according to this preferred embodiment of the invention which are complementary to a polynucleotide as described above may also be used for repression of expression of a gene comprising such a polynucleotide, for example due to an antisense or triple helix effect or for the construction of appropriate ribozymes (see, e.g., EP-B1 0 291 533, EP-A1 0 321 201, EP-A2 0 360 257) which specifically cleave the (pre)-mRNA of a gene comprising a polynucleotide of the invention. Selection of appropriate target sites and corresponding ribozymes can be done as described for example in Steinecke, Ribozymes, Methods in Cell Biology 50, Galbraith et al. eds Academic Press, Inc. (1995), 449-460. Standard methods relating to antisense technology have also been described (Melani, Cancer Res. 51 (1991), 2897-2901). Said nucleic acid molecules may be chemically synthesized or transcribed by an appropriate vector containing a chimeric gene which allows for the transcription of said nucleic acid molecule in the cell. Such nucleic acid molecules may further contain ribozyme sequences as described above.

In this respect, it is also to be understood that the polynucleotide of the invention can be used for "gene targeting" and/or "gene replacement", for restoring a mutant gene or for creating a mutant gene via homologous recombination; see for example Mouellic, Proc. Natl. Acad. Sci. USA, 87 (1990), 4712-4716; Joyner, Gene Targeting, A Practical Approach, Oxford University Press.

WO 01/58951 PCT/EP01/01457

-26

Furthermore, the person skilled in the art is well aware that it is also possible to label such a nucleic acid probe with an appropriate marker for specific applications, such as for the detection of the presence of a polynucleotide of the invention in a sample derived from an organism, in particular mammals, preferably human. A number of companies such as Pharmacia Biotech (Piscataway NJ), Promega (Madison WI), and US Biochemical Corp (Cleveland OH) supply commercial kits and protocols for these procedures. Suitable reporter molecules or labels include those radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles and the like. Patents teaching the use of such labels include US Patents US-A-3,817,837; US-A-3,850,752; US-A-3,939,350; US-A-3,996,345; US-A-4,227,437; US-A-4,275,149 and US-A-4,366,241. Also, recombinant immunoglobulins may be produced as shown in US-A-4,816,567 incorporated herein by reference.

Furthermore, the so-called "peptide nucleic acid" (PNA) technique can be used for the detection or inhibition of the expression of a polynucleotide of the invention. For example, the binding of PNAs to complementary as well as various single stranded RNA and DNA nucleic acid molecules can be systematically investigated using thermal denaturation and BIAcore surface-interaction techniques (Jensen, Biochemistry 36 (1997), 5072-5077).

20

25

30

35

5

10

15

The present invention also relates to a method for the production of a transgenic non-human animal, preferably transgenic mouse, comprising introduction of a polynucleotide or vector of the invention into a germ cell, an embryonic cell, stem cell or an egg or a cell derived therefrom. The non-human animal can be used in accordance with a screening method of the invention described herein. Production of transgenic embryos and screening of those can be performed, e.g., as described by A. L. Joyner Ed., Gene Targeting, A Practical Approach (1993), Oxford University Press. The DNA of the embryonal membranes of embryos can be analyzed using, e.g., Southern blots with an appropriate probe; see supra. The invention also relates to transgenic non-human animals such as transgenic mouse, rats, hamsters, dogs, monkeys, rabbits, pigs, C. elegans and fish such as Torpedo fish comprising a polynucleotide or vector of the invention or obtained by the method described above, preferably wherein said polynucleotide or vector is stably integrated into the genome of said non-human animal, preferably such that the presence of said polynucleotide or vector leads to the expression of the water-soluble protein of the present invention.

WO 01/58951 PCT/EP01/01457

-27

The present invention further relates to composition comprising any one of the above described water-soluble ligand-binding proteins, multimers such as dimers or pentamers thereof, ligand-gated ion channels, polynucleotides, vectors, host cells, antigens, antibodies, or oligonucleotide probes of the invention; and optionally suitable means for detection or performing a ligand-receptor binding assay. In this context, the present invention also relates to a method for identifying an agonist/activator or antagonist/inhibitor of a ligand-gated receptor comprising the steps of:

- (a) contacting the water-soluble ligand-binding protein of the present invention, multimers such as dimers or pentamers thereof, or the ligand-gated ion channel of the invention or a cell expressing said protein in the presence of components capable of providing a detectable signal in response to ligand binding with a compound to be screened under conditions that permit binding of said compound to the ligand-binding protein; and
- 15 (b) detecting the presence or absence of a signal generated from the binding activity of the ligand-binding protein, wherein the presence/increase and absence/decrease of the signal is indicative for an agonist/activator and antagonist/inhibitor, respectively, of a ligand-gated receptor.
- Since ligand-gated receptors are modulated allosterically by natural polyamines, 20 such as spermine, and by polyamine derivatives, such as polyamine amides (e.g. methoctramine) and polymethylene tetraamines (e.g. philanthotoxin-343) (Usherwood, Farmaco. 55 (2000), 202-205) compounds comprising or based on such entities may be used as starting material for screening. An antagonist or agonist that "modulates the activity" of a polypeptide and causes an altered signal, for 25 example response in the cell refers to a compound that alters the activity of the protein so that it behaves differently in the presence of the compound than in the absence of the compound. Typically, the effect of an antagonist is observed as a blocking of agonist-induced receptor activation. Antagonists include competitive as well as non-competitive antagonists. A competitive antagonist (or competitive 30 blocker) interacts with or near the site specific for agonist binding. A non-competitive antagonist or blocker inactivates the function of the receptor by interacting with a site other than the agonist interaction site. As understood by those of skill in the art, bloassay methods for identifying compounds that modulate the activity of receptors such as proteins of the invention generally require comparison to a control. One type 35 of "control" is a cell or culture that is treated substantially the same as the test cell or test culture exposed to the compound, with the distinction that the "control" cell or

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-28

culture is not exposed to the compound. For example, in methods that use voltage clamp electrophysiological procedures, the same cell can be tested in the presence or absence of compound, by merely changing the external solution bathing the cell. Accordingly, the response of the transfected cell to the "control" cell or culture to the same compound under the same reaction conditions. However, "control data" can also be used from the literature.

As described in Example 6 the 3-dimensional structure of AChBP could be solved by X-ray crystallography at 2.7Å resolution (current Rfactor = 27.9 %, Rfree = 30.0 %). In crystals, as in solution, AChBP forms a stable homo-pentamer with dimensions comparable to those of the ligand-binding domain of ligand-gated ion channels, in particular comparable to the nAChR, as determined in EM studies by Unwin and coworkers; see supra. The structural analysis revealed that in the AChBP homopentamer the monomers have immunoglobulin-like topology. At each of five subunit interfaces a ligand-binding site is located, with all residues consistent with biochemical data. In this site a buffer molecule (HERPES) stacks with cation- π interactions on a tryptophan, resembling acetylcholine binding. The AChBP structure is relevant for the development of drugs against, *e.g.*, Alzheimer's disease and nicotine addiction. The high-resolution crystal structure of AChBP, along with biochemical and pharmacological data, supports the teaching of the present invention that the water-soluble ligand-binding proteins of the invention such as AChBP are good mimics of ligand-binding domains of ligand-gated ion channels.

Thus, the present invention relates to a crystal of a water-soluble ligand-binding protein of the invention, preferably in a multimeric form such as dimer, pentamer or decamer. In one embodiment said crystal comprises a protein-ligand complex. Methods how to employ and analyze such crystals are known to the person skilled in the art; see for example US-A-5,872,011 which describes the crystal structure of a protein-ligand complex containing an N-terminal truncated eIF4E and uses thereof. The crystal structure of the ligand-gated receptor ligand-binding region in a complex with a ligand, preferably being an antagonist or agonist will reveal the determinants of receptor-antagonist/agonist interactions and how ligand-binding specificity and affinity are altered by remote residues and the redox state of the conserved disulphide bond. The structure may also indicate mechanisms for allosteric effector action and for ligand-induced channel gating. How the information on the crystal structure of a ligand-binding region in a complex with a ligand can be used for the development of agonists and antagonists has been described for the structure of a

15

20

25

WO 01/58951 PCT/EP01/01457

-29

glutamate-receptor ligand-binding core in complex with kainate (Armstrong et al., Nature 395 (1998), 913-917).

The crystal of the invention, in particular when comprising nAChR related proteins can be a complex of the protein with a ligand comprising an N-alkylated hydroxyalkyl and/or a quaternary ammonium ion. However, other ligands my be used as well. Preferred ligands comprise 4-(2-Hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES), B-bippinatin, lophotoxin, d-tubocurarine, nicotine, acetylcholine, conotoxin, carbamylcholine, galanthamine, epibatidine or alpha-bungarotoxin or derivatives thereof.

Different aspects of X-ray crystallography are such as data collection, structure solution, determining the molecular structure from X-ray diffraction, refinement, etc. are described in the prior art, see, e.g., Powell, Annu. Rep. Prog. Chem., Sect. C: Phys. Chem. 96 (2000), 139-175 and Methods in Enzymology, 276-277, edited by Carter and Sweet, Academic Press, 1997. Current methods and optimization algorithms for the refinement of X-ray crystal structures are described by Van Der Maelen Uria, Crystallogr. Rev. 7 (1999), 125-180.

The crystal of the invention effectively diffracts X-rays for the determination of the atomic coordinates of the protein or protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms. In a preferred embodiment the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 3.0 Angstroms. In a more preferred embodiment the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 2.0 Angstroms. In one embodiment the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of about 2.7 Angstroms.

Preferably, the crystal of the invention is formed by a protein that has an amino acid sequence of amino acids 20 to 223 of SEQ ID No. 2, or an amino acid sequence that differs from amino acid 20 to 223 of SEQ ID No. 2 by only having conservative substitutions. As is described in the examples, the crystals of the AChBP comprise decameric forms of the protein. In order to ease the use of the AChBP protein for analysis and crystallography it is envisaged to create a mutation in residue Asp2 and Asp5 of the mature AChBP SEQ ID No. 2 or 4 to remove the calcium binding site, and prevent creation of a decamer. This deletion can be done for example by

10

15

20

25

30

WO 01/58951 PCT/EP01/01457

-30

oligonucleotide-directed mutagenesis. Alternatively crystals could be grown in a low calcium concentration or in the absence of calcium.

The crystal of the present invention preferably has (1) a space group of $P2_12_12_1$ and a unit cell of dimensions of a=120.6Å, b=137.0Å and c=161.5Å; (2) a space group of $P4_22_12$ and a unit cell of dimensions of a=b=141.6Å and c=120.8Å or (3) a space group of $P2_1$ and a unit cell of dimensions of a=121.1Å, b=162.1Å, c=139.4Å, $\beta=90.1^\circ$.

The crystal of the present invention is preferably from a protein that has secondary structural elements that include .alpha.-helix and antiparallel .beta.-sheets as shown in and described for Figures 7, 10, 11 and/or 12. Most preferably, the crystal of the invention has a three-dimensional structure as defined by atomic coordinates shown in Table 1. Those of skill in the art understand that a set of structure coordinates determined by X-ray crystallography is not without standard error. For the purpose of this invention, any set of structure coordinates for AChBP or AChBP mutants that have a root mean square deviation of protein backbone atoms (N, C.alpha., C and O) of less than 0.75 Angstrom when superimposed - using backbone atoms - on the structure coordinates listed in Table 1 shall be considered identical.

In a most preferred embodiment of the present invention, the crystal has a binding cavity as shown in Figures 6, 8, 9 and/or 13.

In accordance with the findings of the present invention, it is proposed to use the water-soluble ligand-binding proteins of molluscs as the blueprint for the receptor binding site of the ligand-gated ion channel superfamily including nACh, 5-HT3, glycine, GABAA, and GABAC, most preferably for the nAChR. The availability of X-ray structures, and the cloned sequences provide a unique opportunity to understand these receptors at the molecular level, possibly unravel the dynamic changes occurring upon ligand binding, and predict their tertiary and quaternary structure with a higher degree of confidence than possible for other protein modules. This should pave the way for designing ligands selective for any of the multiple subtypes in any of these receptor families. The AChBP-like structures can be used for computerized docking to homology models which leads to the *a priori* discovery of novel ligands before laboratory experiments begin to optimize the drug candidates.

Thus, the present invention also relates to a method of using the crystal of the invention in a drug screening assays, such as comprising:

35 (a) selecting a potential ligand by performing structure assisted drug design with the three-dimensional structure determined for the crystal,

15

20

25

WO 01/58951 PCT/EP01/01457

-31

- wherein said selecting is performed in conjunction with computer modeling; optionally
- (b) contacting the potential ligand with the ligand binding domain of the ligand-gated receptor in an in vitro or in vivo assay; and
- 5 (c) detecting the binding of the potential ligand for the ligand binding domain.

The use of macromolecular crystallography as a tool for investigating drug and receptor interactions, in particular structure-based drug design is reviewed in Oakley and Wilce, Clin. Exp. Pharmacol. Physiol. 27 (2000), 145-151. The desired drug could be an inhibitor or an agonist that mimics endogenous transmitters or ligands. Once the 3-D structure of the relevant target is known, computational processes can be used to search databases of compounds to identify ones that may interact strongly with the target. Lead compounds can be improved using the 3-D structure of the complex of the lead compound and its biological target. The activity of the selected compound can then be tested in a functional assay such as one of those described herein.

Preferably, the potential drug is selected on the basis of its having a greater affinity for the ligand binding domain of the ligand-gated receptor than that of a standard ligand for the ligand binding domain of the ligand-gated receptor. However, the affinity of the selected compound may also be less than that of a standard ligand. Such compounds are useful for example as a lead for the development of further analogues which in turn may have enhanced binding affinity or otherwise beneficial therapeutic properties. On the other hand, the selected compound may bind to a site of the ligand-gated receptor other than known ligands. In a preferred embodiment, the ligand-gated receptor is a nicotinic acetylcholine receptor.

In a further embodiment, the method of the present invention further comprises:

- (d) forming a supplemental crystal of a protein-ligand complex by co-30 crystallization or soaking the crystal of the water-soluble ligand-binding protein with a potential drug, wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms, more preferably greater than 3;
- 35 (e) determining the three-dimensional structure of the supplemental crystal;

WO 01/58951 PCT/EP01/01457

-32

- (f) selecting a candidate drug by performing a structure assisted drug design with the three-dimensional structure determined for the supplemental crystal, wherein said selecting is performed in conjunction with computer modeling; optionally
- 5 (g) contacting the candidate drug with a cell that expresses the ligandgated receptor; and
 - (h) detecting a cell response; wherein a candidate drug is identified as a drug when the cell response is altered compared to a cell that has not been contacted with the candidate compound.
- The above described methods can further comprise an initial step that precedes step

 (a) wherein said initial step consists of determining the three-dimensional structure of
 a crystal comprising a protein-ligand complex formed between the water-soluble
 ligand-binding protein, and the ligand of the ligand-gated receptor, wherein the
 crystal effectively diffracts X-rays for the determination of the atomic coordinates of
 the protein-ligand complex to a resolution of greater than 5.0, preferably greater than
 4.0 Angstroms. Preferably, the resolution of crystal diffraction in the above described
 methods is at least 3.0, most preferably at least about 2.7 Angstroms.

In a still further embodiment, the present invention relates to a method of growing a crystal of a protein-ligand complex comprising:

- (a) contacting the water-soluble ligand-binding protein described above with a ligand of a ligand-gated receptor, wherein the water-soluble ligand-binding protein forms a protein-ligand complex with the ligand; and
- (b) growing the crystal of the protein-ligand complex; wherein the
 crystal effectively diffracts X-rays for the determination of the
 atomic coordinates of the protein-ligand complex to a resolution
 of greater than 5.0, preferably greater than 4.0 Angstroms, more preferably at
 least 3.0, most preferably at least about 2.7 Angstroms.
- The crystals of the present invention can also be used in X-ray crystallography-driven screening technique that combines the steps of lead identification, structural assessment, and optimization such as described for example in Nienaber et al., Nature Biotechnol. 18 (2000), 1105 1108. This crystallographic screening method (named CrystaLEAD) has been used to sample large compound libraries and detecting ligands by monitoring changes in the electron density map of the crystal relative to the unbound form. The electron density map yields a high- resolution picture of the ligand-protein complex that provides key information to a structure-

WO 01/58951 PCT/EP01/01457

-33

directed drug discovery process. The bound ligand is directly visualized in the electron density map. Ligands that bind away from the targeted site may be eliminated.

The above described methods can be coupled with state-of-the-art laboratory data collection facilities including CCD detectors and data acquisition robotics.

Further embodiments that may be used in accordance with the ligand-binding proteins and receptor of the present invention are described in the prior art, for example ligand screening and design by X-ray crystallography is disclosed in WO99/45379 and WO99/45389; WO00/14105 describes assaying a candidate compound for its ability to interact with a modified receptor tyrosine kinase including obtaining and applying crystallography coordinates to a computer algorithm for generating a model which is applied in an iterative process to various molecular structures in order to identify agonist and antagonists of the receptor. All these methods may be equally applied to the proteins and crystals of the present invention.

15

20

10

In one preferred embodiment, the present invention relates to a drug screening assay comprising soaking a crystal of the invention in a solution of compounds to be screened and detecting the binding of the compound to the ligand-binding protein. A possible procedure is also described in Example 9. Besides the detection methods of ligand-binding mentioned above, in the cited documents and in the examples, the detection can also be based on measuring the release of the ligand in the preformed crystal of a protein-ligand complex. As described herein before, said ligand preferably comprises an alkylated nitrogen and/or quaternary ammonium ion or may be one of those described above.

25

30

35

The structural information on the crystals of the present invention can also be used for increasing or decreasing the affinity of a drug to a ligand-gated receptor. Such a method can comprise performing structure assisted drug design with the three-dimensional structure determined for the crystal, wherein said drug design is performed in conjunction with computer modeling; and modifying said drug to alter or eliminate a portion thereof suspected of interacting with a binding site of the binding cavity or with a non-specific binding site of the protein in the crystal. This method can, of course, be combined with one or more steps of any of the above described screening methods or other screening methods well known in the art. Methods for clinical compound discovery comprises for example ultrahigh-throughput screening (Sundberg, Curr. Opin. Biotechnol. 11 (2000), 47–53) for lead identification, and structure-based drug design (Verlinde and Hol, Structure 2 (1994), 577–587) and

WO 01/58951 PCT/EP01/01457

-34

combinatorial chemistry (Salemme et al., Structure 15 (1997), 319-324) for lead optimization. Further information that could be taken into account for drug selection and design so far available for the localization of agonist and competitive antagonist binding sites on nicotinic acetylcholine receptors have recently been reviewed (Arias, Neurochem. Int. 36 (2000), 595-6450; Corringer et al., 1999). Once a drug has been selected, the method can have the additional step of repeating the method used to perform rational drug design using the modified drug and to assess whether said modified drug displays better affinity according to for example interaction/energy analysis.

10

15

20

25

A related method of the present invention for drug design comprises the step of using the structural coordinates of the water-soluble ligand-binding protein crystal comprising the coordinates of Table 1, to computationally evaluate a chemical entity for associating with the ligand-binding site or a non-specific binding site of a ligandbinding protein. This approach, made possible and enabled by this invention, is to screen computationally small molecule data bases for chemical entities or compounds that can bind in whole, or in part, to the AChBP. In this screening, the quality of fit of such entities or compounds to the binding site may be judged either by shape complementarity or by estimated interaction energy. Meng, et al., J. Coma. Chem. 13 (1992), 505-524. In addition, in accordance with this invention, AChBP mutants or chimerics may be crystallized in co-complex with known ligand-gated ion channel inhibitors. The crystal structures of a series of such complexes may then be solved by molecular replacement (for review see for example Brunger er al. Prog. Biophys. Mol. Biol. 72 (1999), 135-155; and references cited therein) and compared with that of wild-type AChBP. Potential sites for modification within the various binding sites of the ligand-binding domain may thus be identified. This information provides an additional tool for determining the most efficient binding interactions, for example, increased hydrophobic interactions, between AChPB and a chemical entity or compound.

The design of compounds that bind to or inhibit ligand-gated ion channels according 30 to this invention generally involves consideration of two factors.

First, the compound must be capable of physically and structurally associating with the ligand-binding domain. Non-covalent molecular interactions important in the association of the ligand-binding domain with its ligand include hydrogen bonding,

van der Waals and hydrophobic interactions. 35

> Second, the compound must be able to assume a conformation that allows it to associate with the ligand-binding domain. Although certain portions of the compound

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-35

will not directly participate in this association, those portions may still influence the overall conformation of the molecule. This, in turn, may have a significant impact on potency. Such conformational requirements include the overall three-dimensional structure and orientation of the chemical entity or compound in relation to all or a portion of the binding site or the spacing between functional groups of a compound comprising several chemical entities that directly interact with the AChBP.

If the theoretical structure of the given compound suggests insufficient interaction and association between it and AChBP, synthesis and testing of the compound is obviated. However, if computer modelling indicates a strong interaction, the molecule may then be synthesized and tested for its ability to bind to AChPB or a ligand-gated ion channel and functionally tested according to the methods mentioned above. In this manner, synthesis of inoperative compounds may be avoided. Once suitable chemical entities or fragments have been selected, they can be assembled into a single compound or inhibitor. Assembly may be proceed by visual inspection of the relationship of the fragments to each other on the three-dimensional image displayed on a computer screen in relation to the structure coordinates of AChBP. This would be followed by manual model building using software such as Quanta or Sybyl. Useful programs to aid one of skill in the art in connecting the individual chemical entities or fragments include CAVEAT (Bartlett, et al, "CAVEAT: A Program to Facilitate the Structure-Derived Design of Biologically Active Molecules". In Molecular Recognition in Chemical and Biological Problems", Special Pub., Royal Chem. Soc. 78 (1989), 182-196); 3D Database systems such as MACCS-3D (Martin, J. Med. Chem. 35 (1992), 2145-2154) and HOOK (Molecular Simulations, Burlington, Mass.). Instead of proceeding to build an AChBP ligand in a step-wise fashion one fragment or chemical entity at a time as described above, AChBP binding compounds may be designed as a whole or "de novo" using either an empty active site or optionally including some portion(s) of a known ligand(s). These methods include LUDI (Bohm, J. ComR. Aid. Molec. Design 6 (1992), 61-78); LEGEND (Nishibata and Itai, Tetrahedron 47 (1991), 8985); and LeapFrog (Tripos Associates, St. Louis, Mo.). Other molecular modelling techniques may also be employed in accordance with this invention; see, e.g., Cohen, J. Med. Chem. 33 (1990), 883-894 and Navia and Murcko, Current Opinions in Structural Biology 2 (1992), 202-210.

Methods for the identification of drugs or corresponding lead compounds in computational prescreen using X-ray crystal structures are described in the prior art

Such computer modeling is preferably performed with a Docking program (Dunbrack

et al., Protein Sci. 6 (1997), 1661-1681 and Folding Des. 2 (1997), R27-R42).

-36

(Verlinde and Hol, Structure 2 (1994), 577–587; Kuntz, Science 257 (1992), 1078–1082; Shuker et al., Science 274 (1996), 1531–1534; Fejzo et al., Chem. Biol. 6 (1999), 755–769; WO 98/58961). The structural information can be consulted to efficiently optimize leads. Computational programs have been written to identify compounds ranging from very small molecules or functional groups (GRID: Goodford, J. Med. Chem. 28 (1985), 849–857; MCSS: Cafilsh et al., J. Med. Chem. 36 (1993), 2142–2167) to potential lead scaffolds (DOCK: Kuntz et al., Accounts Chem. Res. 27 (1994), 117–123) using solved X-ray crystal structures. Another method computationally prescreens compound libraries and experimentally tests the individual "hits" by X-ray crystallography (Verlinde et al., J. Comput. Aided Mol. Des. 6 (1992), 131–147) in order to decrease the size of the screening library. In addition, an experimental approach has been developed to find organic solvents that bind to active sites that may be recombined into a lead macromolecule (Allen et al., J. Phys. Chem. 100 (1996), 2605–2611).

15

20

25

10

5

Once a compound has been designed or selected by the above methods, the efficiency with which that compound may bind to the AChBP or a corresponding ligand-binding domain may be tested and optimized by computational evaluation. For example, a compound that has been designed or selected to function as an inhibitor must preferably demonstrate a relatively small difference in energy between its bound and free states (i.e., a small deformation energy of binding). Thus, the most efficient inhibitors should preferably be designed with a deformation energy of binding of not greater than about 10 kcal/mole, preferably, not greater than 7 kcal/mole. Inhibitors may interact with the ligand-binding domain in more than one conformation that is similar in overall binding energy. In those cases, the deformation energy of binding is taken to be the difference between the energy of the free compound and the average energy of the conformations observed when the inhibitor binds to the AChBP.

A compound designed or selected as binding to AChBP may be further computationally optimized so that in its bound state it would preferably lack repulsive electrostatic interaction with the target ligand-binding domain. Such non-complementary (e.g., electrostatic) interactions include repulsive charge-charge, dipole-dipole and charge-dipole interactions. Specifically, the sum of all electrostatic interactions between the ligand and the AChBP when the ligand is bound to AChBP, preferably make a neutral or favorable contribution to the enthalpy of binding. Specific computer software is available in the art to evaluate compound deformation

-37

energy and electrostatic interaction. Examples of programs designed for such uses include Gaussian 92, revision C (Frisch, Gaussian, Inc., Pittsburgh, Pa.); AMBER, version 4.0 (Kollman, University of California at San Francisco); QUANTA/CHARMM (Molecular Simulations, Inc., Burlington, Mass.); and Insight II/Discover (Biosysm Technologies Inc., San Diego, Calif.). These programs may be implemented, for instance, using a Silicon Graphics workstation, IRIS 4D/35, IBM RISC/6000 workstation model 550 or better a Unix workstation (SGI, Alpha, Sun, etc.) or any Linux PC. Other hardware systems and software packages will be known to those skilled in the art.

Once an AChBP-binding compound has been optimally selected or designed, as described above, substitutions may then be made in some of its atoms or side groups in order to improve or modify its binding properties. Generally, initial substitutions are conservative, i.e., the replacement group will have approximately the same size, shape, hydrophobicity and charge as the original group. It should, of course, be understood that components known in the art to alter conformation should be avoided. Such substituted chemical compounds may then be analyzed for efficiency of fit to AChBP by the same computer methods described in detail, above. As mentioned before, the above described methods of the present invention can also be used as an initial drug screening assay followed by a classical drug screening assay using the biochemical assays known in the art.

Methods for the preparation of compounds, chemical derivatives and analogues are well known to those skilled in the art and are described in, for example, Beilstein, Handbook of Organic Chemistry, Springer edition New York Inc., 175 Fifth Avenue, New York, N.Y.

25

30

35

20

10

15

In one embodiment of the method of the present invention the identified drug prevents or promotes correct assembly of a ligand-gated ion channel. Thus, the selected drug may for example either interfere with the contact regions of the monomers of the ligand-gated ion channel or may act as a scaffold for the assembly. In the latter case, the drug may be based for example on an antibody which binds to the contact regions of two or more monomers when assembled and thus facilitates the assembly process. Preferred contact regions with respect to the AChBP and the related nicotinic acetylcholine receptor are given below. In a still further embodiment of the above described methods, the drug can be selected such as to bind to a non-specific binding site of a ligand-gated ion channel. The non-specific binding site can for example include those contact regions that are highly conserved between the monomers of the ligand-gated ion channels.

· 10

15

20

25

30

35

-38

Once a drug has been selected in accordance with any one of the above described methods of the present invention, the drug or a pro-drug thereof can be synthesized in a therapeutically effective amount. As used herein, the term "therapeutically effective amount" means the total amount of the drug or pro-drug that is sufficient to show a meaningful patient benefit, i.e., treatment, healing, prevention or amelioration of a condition related to an ligand-gated ion channel, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. In addition or alternatively, in particular with respect to pre-clinical testing of the drug the term "therapeutically effective amount" includes the total amount of the drug or pro-drug that is sufficient to elicit a physiological response upon its binding to its target ligand-gated ion channel in an non-human animal test.

The present invention also relates to a drug produced by any one of the above described methods of the present invention, or a pro-drug thereof. Preferably, the drug or pro-drug thereof is present either alone or in a composition in a therapeutically effective amount.

The drug obtained by a method of the present invention may be characterized by its interaction with the binding sites in the binding cavity defined by the coordinates of crystal structure of the protein-ligand complex; for examples of such characterization see, e.g., US-A-5,798,247. Preferably, the drug, for example a potential inhibitor will form non-covalent bonds with one or more amino acids in the active site based upon the crystal structure. On the other hand, the drug may bind to a contact region of the individual monomers of the pentameric ligand-gated receptor. For example, multimer contact regions in *Lymnaea stagnalis* AChBP (SEQ ID No. 2) have been identified. Consecutive regions have at least every second residue involved in contacts with the other monomer. Contacts have been defined as 2 atoms within 4.2 angstrom distance in 2.7 Angstrom structure. The primary contact regions in mature AChBP (residues from A contacting B) are 15-21, 44-47, 85-87, 91-94, 122-124,143-146, 149, 185-187 and the complementary contact regions (from B contacting A, (identical to residues on A contacting E) are 3-4, 7-8, 11, 37-39, 53, 75-77, 96-104, 114-118, 163-170: see also Figure 14.

Thus, in one preferred embodiment the drug of the present invention interacts with a ligand-gated receptor comprising a pentamer with monomers A to E, wherein the drug binds to one or more primary contact regions of a monomer (residues from A contacting B) defined by amino acid residues 15 to 21, 44 to 47, 85 to 87, 91 to 94, 122 to 124, 143 to 146, 149, 185 to 187 of SEQ ID No. 2 and/or to one or more of the

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-39

complementary contact regions of the other monomer (from B contacting A, (identical to residues on A contacting E) defined by amino acid residues 3 to 4, 7 to 8, 11, 37 to 39, 53, 75 to 77, 96 to 104, 114 to 118 and 163-170 of SEQ ID No. 2; or to one of the contact regions identified in Figure 14; or to the corresponding contact regions of the monomers of a ligand-gated ion channel. Preferably, the ligand-gated lon channel is the nicotinic acetylcholine receptor and the order of the monomers is $\alpha\gamma\alpha\delta\beta$.

Any available method may be used to construct such model from the crystallographic and/or amino acid sequence data disclosed herein or obtained from independent analysis of crystalline AChBP proteins or other water-soluble ligand-binding proteins of the present invention. Such a model can be constructed from available analytical data points using known software packages such as HKL, MOSFILM, XDS, CCP4, SHARP, PHASES, HEAVY, XPLOR, TNT, NMRCOMPASS, NMRPIPE, DIANA, NMRDRAW, FELIX, VNMR, MADIGRAS, QUANTA, BUSTER, SOLVE, O, FRODO, RASMOL, CNS , REFMAC, ARP/WARP, XTALVIEW and CHAIN. The model constructed from these data can then be visualized using available systems, including, for example, Silicon Graphics, Evans and Sutherland, SUN, Hewlett Packard, Apple Macintosh, DEC, IBM, and Compaq. The present invention also provides for devices such as a computer system which comprises the model of the invention and hardware used for construction, processing and/or visualization of the model of the invention. Further embodiments provide a computer system comprising computer hardware and the model of the present invention. The study of the interaction of the candidate species with the model can be performed using available software platforms, including QUANTA, RASMOL, O, CHAIN, FRODO, INSIGHT, DOCK, MCSS/HOOK, CHARMM, LEAPFROG, CAVEAT (UC Berkley), CAVEAT (MSI), MODELLER, CATALYST, XTALVIEW and ISIS. Computer readable media such as floppy discs, CD ROMs, tapes, and any other storage or processing means comprising crystallographic and/or nucleotide/amino acid sequence data disclosed herein or obtained from independent analysis of crystalline AChBP proteins or other water-soluble ligand-binding proteins of the present invention are subject of the present invention as well. Any one of the mentioned means and devices can advantageously be used for modeling an antagonist/inhibitor or agonist/activator of a ligand-gated receptor.

Furthermore, the present invention relates to the construction of theoretical three dimensional (3D) models of ligand-binding domains of ligand-gated ion channels by computer-assisted molecular modeling using the X-ray coordinates of the water-soluble ligand-binding proteins of the invention. These 3D models can correspond

-40

either to the entire ligand-binding domain (~220 to 240 extracellular amino acids) or may be limited to the ligand-binding site.

The concept of using 3D structures of the mollusc ligand-binding proteins for molecular modeling and tool for structure prediction of for example mammalian, in particular human ligand-gated ion channels gains support from the observation that the ligand-binding domain of vertebrate glutamate receptor channels and bacterial periplasmic substrate-binding proteins (PBPs) share similar 3D structures despite the very low sequence similarity between ionotropic glutamate receptor subunits and the PBPs that were used as templates (12%); for review see Paas et al. TiPS 21 (2000),

10 87- 92 and refernces cited therein

15

20

25

30

35

Thus, on the basis of a computer-assisted molecular modeling, optionally supplemented by for example functional studies of site-specific mutants, the crystal structure of the ligand-binding domain of ligand-gated ion channels and theoretical 3D models of these domains can be predicted. In turn, these models can be used for structure assisted drug design. The predicted models may be further refined, for example by monitoring the effects of mutations of amino acid residues that are probably located in the ligand-binding site on (1) agonist-elicited channel activation and desensitization, (2) inhibition of channel activity by various competitive receptor antagonists; or (3) the binding of various ligands. Experimental setups for analyzing such effects are known to the person skilled in the art, see also the documents cited for functional assay systems of ligand-gated ion channels.

Thus, the embodiments of the present invention enable various possibilities for identification and modeling new ligands of ligand-gated ion channels as well as modifying the ion channels themselves. Accordingly, the present invention relates to the use of the above described polynucleotides, proteins, dimers and pentamers, ligand-gated ion channels, vectors, host cells, antigens, antibodies, oligonucleotide probes, crystals, their structural coordinates and methods for screening or profiling putative ligands of ligand-gated receptors.

Methods for the lead generation in drug discovery using proteins and detection methods such as mass spectrometry (Cheng et al. J. Am. Chem. Soc. 117 (1995), 8859–8860) and some nuclear magnetic resonance (NMR) methods (Fejzo et al., Chem. Biol. 6 (1999), 755–769; Lin et al., J. Org. Chem. 62 (1997), 8930–8931).

The newly identified drug obtained by a method of the present invention, i.e. an antagonist/inhibitor or agonist/activator can be used for the preparation of a pharmaceutical composition for the treatment of a ligand-gated ion channel mediated or related disorder. Such disorders are well know to the person skilled in the art. For

WO 01/58951 PCT/EP01/01457

-41

example, possible applications of agonist and antagonists to nAChRs are based on their participation in complex functions such as attention, memory, and cognition, and their involvement in the pathogenesis of certain neuropsychiatric disorders (Alzheimer's and Parkinson's diseases, Tourette's syndrome, schizophrenia, depression, etc). For the majority of these disorders, the use of nAChRs' agonists may represent either a prophylactic (esp. for Alzheimer's and Parkinson's diseases) or a symptomatic treatment; for review see for example Mihailescu and Drucker-Colin, Arch. Med. Res. 31 (2000), 131-144.

The medicinal chemistry and molecular biology of GABA-activated ligand-gated ion channels also in terms of agonist and antagonist structural profiles is described in Chebib et al., J. Med. Chem. 43 (2000), 1427-1447.

Glycine receptors and disorders of glycinergic neurotransmission are extensively reviewed in Rajendra et al., Pharmacol. Ther. 73 (1997), 121-146 and Barry et al., Clin. Exp. Pharmacol. Physiol. 26 (1999), 935-936.

The central role of 5-HT3 receptor in CNS disorders and 5-HT3 receptor antagonists are described in Bloom and Morales, Neurochemical Research 23 (1998), 653-659 and Higgins and Kilpatrick, Expert Opin. Invest. Drugs 8 (1999), 2183-2188.

In one embodiment, the antagonist/inhibitor is or is derived from a protein, an antigen, antibody or from a toxin of the ligand-gated ion channel. Likewise, the agonist/activator can be derived from a protein, an antigen, antibody or from a toxin of the ligand-gated ion channel. Possible starting points comprise for example peptide toxins, e.g., conotoxin (IMI) and alpha bungarotoxin, lophotoxins tubocurarine, decamethonium, alpha-cobratoxin, epibatidine, (Bippinatins), acetylcholine, choline, nicotine, carbachol, serotonin or GABA. The structure of these molecules together with that of the crystal of the target ligand-binding domain can be used to model the compound and elucidate side chains, functional groups etc. which may be added, deleted or modified in order to improve for example affinity and/or specificty of the drug or for example make a drug which acts on a different target non-reactive with a certain ligand-gated ion channel.

In a preferred embodiment for the uses according to the present invention, the ligand-gated ion channel is the nicotinic acetylcholine receptor and said mediated or related disorder is Tourette's syndrome, Alzheimer's disease, addiction to nicotine or schizophrenia.

35

20

25

30

As mentioned herein before, this is the first time it could be shown that water-soluble ligand-binding proteins exists in molluscs, which closely resemble the ligand-binding

-42

domain of ligand-gated ion channel of higher mammals. It is expected that similar ligand-binding proteins exist in other molluscan species or even in the lineage the Mollusca, Protostomia, Coelomata, Bilateria, Eumetazoa, Metazoa, Fungi/Metazoa group. Accordingly, the present invention also relates to the use of a ligand of a ligand-gated ion channel for identifying and isolating a water-soluble ligand-binding protein from such species, preferably from a mollusc. Preferably, the ligand used for the isolation of the protein is α -bungarotoxin. The water-soluble ligand binding proteins obtainable from these organisms as well as derivatives that can be made in accordance with the teaching present herein are also subject of the present invention.

Furthermore, for the first time the crystal structure of a nicotinic binding site has been revealed. This crystal structure shows that the molluscan AChBP is a homolog of the LGIC superfamily ligand binding domains. It reveals the Ig-topology, the location of the binding site at the subunit interface, the position of the MIR and the extensive data on the nicotinic ligand binding residues. Importantly, it gives important new information about the exact fold and the arrangement of the nicotinic ligand-binding site in three dimensions. It shows the presence of a second pocket that has been noticed by EM analysis. Furthermore, it clarifies the arrangement of subunits by showing the relative positioning of the principal and complementary part of the ligand-binding site. It provides an explanation of the role of the LGIC superfamily conserved residues in stabilizing the monomer structure by the formation of hydrophobic cores and packing of secondary structure elements and it makes clear how the pentamers are built up, and how weakly the pentamer interfaces are conserved between LGICs.

This structure can be used for the numerous drug-design studies that are targeting the LGIC superfamily. The general structural knowledge on its folding will be applicable to the GABA, serotonin (5HT₃) and glycine receptor fields. It will help to understand their ligand-binding characteristics and could thus have impact on development of e.g. anti-emetics aimed at the 5HT₃ receptor or the mood-defining drugs that target the GABA receptors. However, the availability of a three-dimensional description of the nicotinic ligand-binding site will be especially relevant for the design of new drugs against Alzheimers' disease, epilepsy and the addiction to smoking which have the neuronal nicotinic receptors as their targets.

35

10

15

20

25

30

Many embodiments and the examples feature the acetylcholine-binding protein (AChBP) of the invention and the embodiments generally described herein are

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-43

preferably related to the nicotinic acetylcholine receptor (nAChR), more preferably to the alpha subunit, and most preferably to the alpha 7 subunit. However, it should be understood that all embodiments equally apply to the other water-soluble ligand-binding proteins and generally to the ligand-gated ion channels mentioned herein. For example, the crystal structure of the AChBP can be used to model new ligands for the acetylcholine receptor, preferably such with inhibiting or stimulating action on the acetylcholine receptor. Likewise, it is possible to identify and model new ligands for other ligand-gated ion channels (including glycine, GABA and serotonin receptor) with inhibiting action. Such ligands may for example prevent correct assembly of ligand gated ion channels. Preferably such ligands prevent correct assembly of specific sub types of ligand gated ion channels. On the other hand, ligands can be identified and modeled that promote correct assembly of ligand gated ion channels, preferably of specific sub types of ligand gated ion channels. As mentioned before, the methods of the present invention also allow modeling inhibitors for the non-specific binding site of ligand gated ion channels.

In addition, it is possible to predict and create mutants and chimeras of AChBP with modified assembly behaviour, modified ligand binding behavior such as with increased resemblance of the binding site to the acetylcholine receptor subtype on the primary binding site and generally with increased resemblance to particular ligand-gated ion channels in activity and conformational changes. In view of the closest relationship between AChBP and the acetylcholine receptor it is particular preferred to create mutants and chimeras with increased resemblance of the binding site to the acetylcholine receptor subtype on the secondary binding site. However, the prediction and creation of mutants and chimeras with increased resemblance of the binding site to other ligand gated ion channels subtype on the primary binding site or on the secondary binding site are envisaged as well.

These and other embodiments are disclosed and encompassed by the description and Examples of the present invention. Further literature concerning any one of the antibodies, methods, uses and compounds to be employed in accordance with the present invention may be retrieved from public libraries and databases, using for example electronic devices. For example the public database "Medline" may be the Internet. for example under available on which is http://www.ncbi.nlm.nih.gov/PubMed/medline.html. **Further** databases and http://www.ncbi.nlm.nih.gov/, http://www.infobiogen.fr/, addresses. such as http://www.fmi.ch/biology/research_tools.html, http://www.tigr.org/, are known to the person skilled in the art and can also be obtained using, e.g., http://www.lycos.com.

-44

An overview of patent information in biotechnology and a survey of relevant sources of patent information useful for retrospective searching and for current awareness is given in Berks, TIBTECH 12 (1994), 352-364.

- This disclosure may best be understood in conjunction with the accompanying drawings, incorporated herein by references. Furthermore, a better understanding of the present invention and of its many advantages will be had from the following examples, given by way of illustration and which are not intended as limiting.
- Unless stated otherwise in the examples, all recombinant DNA techniques are performed according to protocols as described in Sambrook et al. (1989), Molecular Cloning: A Laboratory Manual. Cold Spring Harbor Laboratory Press, NY or in Volumes 1 and 2 of Ausubel et al. (1994), Current Protocols in Molecular Biology, Current Protocols. Standard materials and methods for plant molecular work are described in Plant Molecular Biology Labfase (1993) by R.D.D. Croy, jointly published by BIOS Scientific Publications Ltd (UK) and Blackwell Scientific Publications (UK).

20 Brief description of the drawings

25

30

35

Figure 1: Clustal X (1.8) multiple sequence alignment of AChBP amino acid sequences. The AChBP alignment was made using "ClustalX_1.8" (Thompson et al., Nucleic Acids Research 24 (1997), 4876-4882. The subsequent alignment was further processed using "Genedoc" version 2.5.000 (Nicholas et al. (1997) Genedoc a tool for editing and annotating multiple sequence alignments). Identical amino acids are indicated with "*", equivalent amino acid with ":", and similar amino acids with ".". Glycosylation sites are Asn 66 for L-AChBP and Asn 21 and 26 for B-AChBP in the amino acid sequence of the respective mature AChBP SEQ ID No. 2 and 4, and 6 and 8, respectively.

Figure 2: Hydrophobicity plots of the mature AChBP amino acid sequences. The B&L-AChBP hydrophobicity plots were made using "Protein sequence analyses" according to the method described in Kyte and Doolite (J. Mol. Biol. 157 (1982), 105-132). 2A: L-AChBP_T1 (SEQ ID No. 2), 2B: L-AChBP_T2 (SEQ ID No. 4), 2C: B-AChBP_T1 (SEQ ID No. 6), 2D: B-AChBP_T2 (SEQ ID No. 8).

-45

Figure 3:

5

10

Clustal X (1.8) multiple sequence alignment of AChBP amino acid sequences with the amino acid sequences of the ligand-binding domains of the ligand-gated receptors nAChR-α7, GABA_AR-β1, 5-HT3R and GlyR-α1. Sequence alignment and processing was performed as described for Figure 1. The accession numbers of the amino acid sequences used for the alignment are as follows: Human alpha1: Human alpha7: Y08420; Human 5HT3: CAA06442; Human GlyR_alpha1: S12382; Human GABA_b1: NP_000797. A similar sequence alignment can be performed with the corresponding rat (ratnAChRa7_Q05941, rat5HT3R_P35563, sequences ratGABARb1_P15431, ratGlyRa1_p24524) which will give substantially similar if not identical results.

15 **Figure 4:**

Clustal X (1.8) multiple sequence alignment of AChBP amino acid sequences with the amino acid sequences of nAChRs. Sequence alignment and processing was performed as described for Figure 1. The accession numbers of the amino acid sequences used for the alignment are as follows: Human alpha1: ACHUA1; Human alpha2: AAG23253; Human alpha3: A53956; Human alpha4: P43681; Human alpha5: P30532; Human alpha6: Q15825; Human alpha7: Y08420; Human alpha9: CAB65091. A similar sequence alignment can be sequences performed with the corresponding rat rnAChR2_P1238, (ratnAChRa7_Q05941, rnAChRa9_P43144, rnAChRa3_P04757, rnAChRa4_P09483) which will give substantially similar if not identical results.

25

30

20

Figure 5:

Clustal X (1.8) multiple sequence alignment of AChBP amino acid sequences with the amino acid sequences of nAChRs alpha 1 and 7. Sequence alignment and processing was performed as described for Figure 1. The accession numbers of the amino acid sequences used for the alignment are as follows: Human alpha1: ACHUA1; Human alpha7: Y08420. A similar sequence alignment can be performed with

WO 01/58951

PCT/EP01/01457

-46

the corresponding rat sequence ratnAChRa7_Q05941 which will give substantially similar if not identical results.

5 **Figure 6:**

10

15

The pentameric structure of AChBP. a In this schematic representation each monomer has a different grey level. Subunits are labeled anticlockwise, with A-B, B-C, C-D, D-E and E-A forming the plus and minus interface side, with the principal and complementary ligand-binding sites respectively (ball-and-stick representation). b Viewing the AChBP pentamer perpendicular to the five-fold axis. The equatorially located ligand-binding site (ball-and-stick representation) is highlighted only in the A (light) and B (dark) interface.

Figure 7:

The AChBP monomer. Ribbon representation of the AChBP monomer. The secondary structure starting from the N-terminus (top) towards the C-terminus (bottom). The monomer is viewed towards the center of the pentamer. In the nAChR, the top would correspond to the N-terminus of the ligand binding domain, pointing towards the synaptic cleft, while the C-terminus would be entering the membrane at the bottom, continuing into the transmembrane domain. The AChBP monomer is built up mainly of β-strands, except for an N-terminal ⟨-helix. It contains 14 β-strands that are organized in the two antiparallel β-sheets, with an immunoglobulin topology. However, in contrast to the classical immunoglobulin fold, the AChBP β-sheets are rotated against each other, forming a small pocket, as visible in Figure 6.

25

20

Figure 8:

The ligand-binding site at dimer interface. Ribbon representation of two neighboring AChBP monomers. Monomer A is shown in grey and monomer B in dark grey. The ligand-binding site is located at the interface between two monomers. As predicted for the nAChRs, the acetylcholine binding site in AChBP occurs at the interface between two neighboring subunits. Similar to the model proposed for the nAChRs, the ligand-binding site is asymmetric, formed mainly by aromatic residues. Residues from mature AChBP monomer A (TyrA89, TrpA143, TyrA185, CysA187, CysA188 and TyrA192) form the principal component, while residue TrpB53 from monomer B

35

WO 01/58951

PCT/EP01/01457

-47

creates the complementary part of the ligand-binding site. There are five identical ligand-binding sites in the AChBP pentamer, similar to the homomeric $\alpha 7$ neuronal receptor.

5 Figure 9:

10

15

20

The ligand binding site. Stereo figure showing the ligand binding site in AChBP, at the interface of two monomers. Residues from mature AChBP monomer A (TyrA89, TrpA143, TyrA185, CysA187, CysA188 and TyrA192) form the principal component, while residue TrpB53 from monomer B creates the complementary part of the ligand-binding site with with additional residues ArgB104, LeuB112 and MetB114. There are five identical ligand-binding sites in the AChBP pentamer, similar to the homomeric α7 neuronal receptor.

Figure 10:

Multiple sequence alignment of AChBP amino acid sequences with indication of secondary structure and solvent accessibility derived from the crystal structure. Alignment of the four molluscan AChBP sequences, with secondary structure and solvent accessibility of the Lymnea stagnalis AChBP-1 indicated from the crystal structure. The Figure was prepared with ESPript (Gouet et al., Bioinformatics. 15 (1999), 305-308), using DSSP (Kabsch and Sander, Biopolymers. 22 (1983), 2577-2637). Under the alignment the solvent accessibility is indicated, white most buried, dark blue most exposed, according to ESPript defaults (blue A> 0.4, cyan 0.1<A<0.4, white A<0.1).

25 Figure 11:

Sequence alignment of AChBP with LGICs. The alignment shows only the N-terminal domain of the LGIC subunits and is based on a multi-sequence alignment of 92 full-length LGIC sequences. Abbreviations used, H and Tca, stand for human and *Torpedo californica*. Secondary structure elements (α : α -helix, β : β -strand, η : 3_{10} -helix) are indicated above the sequence, in accordance with Fig 12a. AChBP shares 23% sequence identity with the ligand-binding domain of human α_7 . The LGIC conserved residues (bold, grey background) are displayed. Beginning and end of the Cys-loop are indicated by a "*". Nicotinic receptor ligand-binding residues on the principal and complementary side are indicated.

35

-48

Figure 12:

Overview of the AChBP monomer structure. a Stereo representation of the AChBP monomer as viewed from outside the pentameric ring. Disulfide bridges are indicated in ball-and-stick representation. In a complete ion-channel the N-terminus would be pointing towards the synaptic cleft, while the C-terminus would enter the membrane at the bottom, continuing into the first transmembrane domain. b Topology diagram of the AChBP monomer. For comparison with Ig-folds the strands have been labeled a-g, showing the additional strand (b') and hairpin (f'-f"). In this structure, strands have been labeled β 1- β 10 with loops (or turns) L1-L10 preceding each strand with the same number. The β 5 strand is broken (β 5- β 5') with internal loop L5', β 6 also has a small break, but is shown continuously; (see Fig. 11). The precise beginnings and ends of strands may change slightly with increasing resolution, but the topology seen here will be highly conserved across the entire family of LGICs.

15

20

10

5

Figure 13:

The ligand-binding site. a Stereo representation of the ligand-binding site in ball-and-stick representation, showing the contribution of the principal A (TyrA89/ α_1 Tyr93), B (TrpA143/ α_1 Trp149) and C (TyrA185/ α_1 Tyr190, CysA187/ α_1 Cys192, CysA188/ α_1 Cys193, TyrA192/ α_1 Tyr198) and the complementary D (TrpB53/ γ Trp55, GlnB55/ γ Glu57), E (ArgB104/ γ Leu109, ValB106/ γ Tyr111, LeuB112/ γ Tyr117, MetB114/ γ Leu119) and F (TyrB164) 'loops'. b Stereo view of the electron density map displaying a HEPES buffer molecule in the ligand-binding site. This experimental density (contoured at 1 σ) is derived from cross-crystal averaging. c Location of the principal ligand-binding residues on the monomer. d Location of the complementary ligand-binding residues on the monomer. (orientation as in Figure 6b)

25

30

Figure 14:

Dimer interface a Stereo figure of the dimer interface. Representation of the interface residues (ball-and-stick) on a schematic secondary structure figure. The figure shows the plus face of subunit A and the minus minus face of subunit B b Dimer interface interactions. Note that due to the low conservation of these interfaces (Fig. 11) the actual interactions will not be conserved in any LGIC interface, but that in all receptors the topological regions are likely to form the interface.

WO 01/58951

PCT/EP01/01457

-49

Figure 15:

Conservation in the LGIC superfamily. Conserved residues are indicated on the top, middle and bottom respectively on the monomer as viewed from the central pore. The hydrophilic conserved residues are indicated in dark. Conserved residues are indicated as viewed from the central pore. Hydrophobic Cluster I: residues 6, 10, 63, 65, 71, 81, 105, 111; Cluster II: residues 20, 27, 29, 31, 58, 82, 84, 86, 140, 150, 152, 195; Cluster III: residues 33, 35, 38, 41, 48, 52, 125, 138, 171, 173, 199, 201. The hydrophilic conserved residues: Asp60, Asp85, Asn90, Gly109, Cys123, Cys136, Lys203. Conserved residues in the ligand binding site: 106, 145, 192. These three and Lys203 are the only conserved residues without structural role in the monomer. Note how very few conserved residues are at the surface. Within the LGIC family the Cys-loop residues are also highly conserved; see bottom, left.

10

10

15

20

30

35

WO 01/58951 PCT/EP01/01457

-50 EXAMPLES

EXAMPLE 1: Isolation of Lymnaea AChBP from the CNS, determination of mass and N-terminal protein sequence

Isolation: 80 CNS of Lymnaea were homogenized in lysis buffer (PBS [16 mM Na2HPO4, 4 mM NaH2PO4, pH 7.4; 150 mM NaCl] 0.5% Nonidet P-40; 0.1% triton, 0.2% tween-20) containing 1 ug/ml aprotinin, 10 ug/ml benzamidine, 0.5 ug/ml leupeptin, 24 ug/ml pefabloc. The CNS lysate was cleared by triplicate centrifugation at 12,000x g for 5 min. Streptavidin-coated magnetic beads (Dynal, Oslo), 5 mg, were saturated with α-bungarotoxin conjugated to Biotin (4 ug) (Molecular Probes, Oxford, UK). These beads were washed in PBS to remove excess α-bungarotoxin, then added to the cleared CNS lysate, and incubated for 1 h. After this, beads were washed 3 times in PBS to remove unbound protein. A control reaction without α-bungarotoxin was performed. Proteins bound to α-bungarotoxin were allowed to elute off in 10 μl of PBS containing 10-4 M nicotine for 1h.

Mass determination: The eluent was separated on a microcolumn LC system was similar to that described previously (Hsieh et al.; Anal. Chem. 70; 1998; 1847-1852). A commercial syringe pump (Perkin-Elmer /ABI, model 140B) was used to deliver a flow rate of 20 μl /min to the column. After loading of sample to the column the flow rate was dropped to 10 μl /min. The eluent was then switched from 0.2% acetic acid to 0.2% acetic acid/ 60% acetonitril in 1 min. Electrospray mass spectra in MS mode were acquired on a Micromass Q-TOF quadropole time-of-flight mass spectrometer equipped with a Z-spray atmospheric pressure ionization source.

25 <u>Protein sequence analysis</u>: For sequence analysis α-bungarotoxin binding protein was extracted using the same procedure, now followed by SDS-PAGE and Western Blotting on PDVF membrane. Sequence analysis was performed with Edman degradation of the 24 kDa blotted protein (apparent MW) using a protein sequencer (ABI, Perkin Elmer).

EXAMPLE 2: Cloning the Lymnaea AChBP cDNA sequence: PCR and screening of a cDNA library

PCR cloning: A degenerate oligonucleotide was synthesized based on the amino acid sequence LDRADILYNI (SEQ ID No. 10), residues 1-10, of AChBP, (5'-CGGATCCGA(TC)(AC)GIGC(GATC)GA(TC)AT(ATC)(TC)T(GATC)TA(TC)AA(TC)A T-3'; SEQ ID No. 11), containing a BamHI restriction site, and used in combination with a primer on the IZAPII lambda vector. PCR was performed on a IZAP II cDNA

PCT/EP01/01457 WO 01/58951

-51

library of the Lymnaea CNS, in a 100 μl reaction volume with 1.0 unit of Super Taq DNA polymerase (Boehringer Mannheim, Germany) in a DNA thermal cycler (Perkin-Elmer Cetus, CT) using 45 cycles of (94 °C, 20 sec; 53 °C, 30 sec; and 72 °C, 1 min. Amplified cDNA was digested with BamHI and EcoRI, separated on agarose gel, and a product of ~900 bp was cloned and sequenced. Library screening: Approximately 20,000 clones of the amplified lambda ZAP II CNS cDNA library were plated at a density of 10⁵ pfu/400 cm² and absorbed to charged Nylon membranes (Boehringer Mannheim, Germany). The AChBP PCR product was used as a random primed probe, labeled with [alfa³²P]dATP (specific activity >10⁹ cpm/mg). Membranes were hybridized in 6x SSC (1x SSC: 0.15 M NaCl and 0.015 M Na-citrate), 0.2% SDS, 5x Denhardts and 10 ug/ml herring sperm DNA at 65 °C for 18 h. The filters were washed in 0.2x SSC, 0.2% SDS, at 65 °C for 30 min, and autoradiographed. Four individual cDNA clones were in vivo excised, and sequenced

using dideoxy chain termination in both orientations. Two types of sequence were obtained, named L-AChBP_T1 and L-AChBP_T2. The signal sequences were determined with "SMART", Simple Modular Architectur Research Tool (V3.1); see Schultz et al., Proc. natl. Acad. Sci. USA 95 (1998), 5857-5864 and Nucleic Acids Res. 28 (2000), 231-234. In case of L-AChBP_T1 (SEQ ID No. 2) the prediction could experimentally be confirmed.

20

25

30

35

15

10

EXAMPLE 3: Lymnaea AChBP-related sequences: cloning of the Bulinus truncatus cDNAs

Total RNA was isolated from Bulinus brain ganglia (CNS), and reverse transcribed into hexanucleotide primed cDNA. Two degenerate oligonucleotides, directed to the forward primer: AChBP_T1 sequence, Lymnaea GCGAATTCGAYACIGARWSIGGNGCNACNTG-3' (SEQ ID No. 12), reverse primer: 5'-GCGAAGCTTCRTCYTCRTAIGCYTCNGCRCARC-3' (SEQ ID No. 13), were used to amplify AChBP-related sequences. PCR was performed on one animal equivalent of CNS cDNA using 150 pmole of each primer under standard conditions for 45 cycles (94'C, 20 sec; 54' C, 30 sec; 72 'C, 1 min). Amplified cDNA was EcoRl/HindIII digested, cloned into EcoRI/HindIII digested pBluescript, and sequenced. The ORFs of the obtained sequences showed a Bulinus AChBP, sequence-related to Lymnaea AChBP, named B-AChBP_T1. This partial cDNA was used to screen a Bulinus brain cDNA library using the same hybridization protocol as described for the cloning of the Lymnaea cDNAs, and yielded two cDNA clones, encoding B-AChBP_T1 and B-AChBP_T2. Sequencing of the cDNAs was performed in both orientations.

-52

EXAMPLE 4: The production of L-AChBP-T1 and -T2 and B-AChBP-T1 and -T2 in the yeast Pichia pastoris and functional characterization

5 Production of recombinant AChBP:

10

15

20

25

30

35

In order to produce L-AChBP_T1 and T2 and B-AChBP_T1 and T2 as recombinant proteins in the Pichia pastoris expression system (Pichia Expression Kit version 3.0, Invitrogen), the DNA sequence encoding the mature form of these proteins (see sequence files) was cloned into the pPIC9 expression vector (Invitrogen). The mature sequences of L-AChBP_T1, T2 and B-AChBP_T1 and T2 were PCR amplified (using Pfu-taq DNA polymerase (Stratagene) in order to avoid introduction of errors into the sequence due to PCR) and restriction sites were added to the primers to allow rapid pPIC9 compatible cloning. The amplified sequence of mature AChBP_T1 was EcoRI inserted into pPIC9, whereas L-AChBP_T2 and B-AChBP_T1 and T2 were Xhol/EcoRI inserted into pPIC9 (the alpha-mating factor cleavage site was fully reconstructed after Xhol digestion).

Constructs with and without an additional C-terminal His-tag (SRGHHHHHH (SEQ ID No. 14) in the case of L-AChBP_T1, EFKDDDDKHHHHHHH (SEQ ID No. 15) otherwise) were generated for each of the AChBP (sub)types. The AChBP/pPIC9 constructs were amplified in E. coli DH5 aF and isolated and purified using the plasmid Maxi Kit (Qiagen). Due to the engineered cleavage site at the N-terminus of the amino acid sequence four additional amino acids (EAEA, SEQ ID No. 16) will precede the N-terminus of the original mature protein. Prior to transfection into Pichia pastoris the constructs were linearised (for protocol see supplier's manual; Pichia Expression Kit version 3.0, Invitrogen) and subsequently purified phenol/chloroform extraction, and ethanol precipitation. Approximately 5 µg of each of the linearised constructs was transformed into freshly prepared electro-competent Pichia pastoris cells and plated onto MD plates (for protocol see supplier's manual; Pichia Expression Kit version 3.0, Invitrogen corporation). Electrocompetent Pichia pastoris cells were aquired according to the protocol provided by Invitrogen. Plates were incubated at 30°C until the appearance of Pichia colonies, which were subsequently analysed for the presence of the correct insert by PCR amplification (for protocol see supplier's manual; Pichia Expression Kit version 3.0, Invitrogen). Colonies containing an homologous recombination with the Pichia genome, carrying the AChBP sequence, were grown in 25 ml of BMGY for 1-2 days (30°C; rotation at 250rpm), after which the cells were centrifuged (10 min., 1500g) and the cell pellet was resuspended into 10 ml of BMMY. Growth (30°C, 250rpm) was continued for an

-53

additional 4 days (day 3-6), during which the expression of AChBP was induced by the addition of 100% methanol (1% of total culture volume) once every 24 hours. At day seven the culture was centrifuged (15 min.; 2000g; 4°C) and the medium was collected. The AChBP expression level of the various cultures was determined by the analyses of a fraction of the collected medium with SDS-polyacrylamide gel electrophoresis (see suppliers manual; Pichia Expression Kit version 3.0, Invitrogen). The cultures that yielded the highest level of AChBP expression were selected and stored as glycerol stocks.

Recombinant AChBP that contained a C-terminal His-tag was isolated and purified from the Picha pastoris medium using Talon metal affinity resin (according to protocol as described within the user manual; Clontech laboratories Inc.). The protein concentration was subsequently analysed using SDS-polyacrylamide gel electrophoresis and reference marker proteins. Polyclonal antibodies have been raised successfully to the recombinant L-AChBP_T1 and B-AChBP_T1 proteins in Balb-C mice. Immune-sera were obtained without crosslinking of the proteins.

Binding characteristics of AChBP:

First the binding curve of α -Bungarotoxin to His-tagged AChBP was determined, and an affinity of 3.5 nM was calculated. Using α -Bungarotoxin in a competitive binding assay ligands of several types of ligand-gated ion channels were then tested on Histagged AChBP, i.e., ACh, serotonin, GABA, glycine, and glutamate. Both ACh and serotonin did compete with α -Bungarotoxin binding at 4.2 mM and 269 mM, IC50s respectively. GABA, Glycine and glutamate did not compete for binding with α -Bungarotoxin. Thus, as predicted by the primary sequence and by subunit structure also the ligand-binding characteristics of AChBP resembled that of a nAChR.

In a second series of competitive binding assays the ligand binding characteristics of AChBP were studied in more detail, now using various agonists and antagonists of the AChRs. Nicotine a classical agonist of the nAChRs, is a high affinity ligand of Histagged AChBP (IC50 98 nM). Epibatidine, a high affinity agonist of the nAChRs, also binds with high affinity to His-tagged AChBP (IC50 1.4 nM), which is even higher than the 58 pM affinity of epibatidine reported for the nAChR (Badio, Mol. Pharmacol. 45 (1994), 563-569). Other cholinergic agonists bind with a lower affinity e.g., decamethonium, carbachol, and choline respectively with IC50s of 4.1 μ M, 43 μ M. and 190 μ M. Summary of affinities indicated in Table 2.

30

10

15

20

WO 01/58951

15

20

25

PCT/EP01/01457

-54

Table 2

	IC50 (μM)	nHill		IC50 (μM)	nHIII
serotonin chollne carbachol acetylcholine	269 ± 67 190 ± 32 43 ± 2.7 4.2 ± 1.1	0.65 ± 0.03 0.91 ± 0.20 0.67 ± 0.05 0.72 ± 0.09	α-cobratoxin atropine decamethonium physostigmine	16.2 ± 0.1 5.25 ± 0.49 4.1 ± 0.3 1.25 ± 0.04	4.08 ± 0.30 1.91 ± 0.23 1.13 ± 0.09 0.66 ± 0.07
nicotine epibatidine	0.098 ± 0.025 0.0014 ± 0.0001	0.78 ± 0.05 0.66 ± 0.04	d-tubocurarine gallamine α-bungarotoxin	0.093 ± 0.003 0.039 ± 0.007 0.0026 ± 0.0006	0.83 ± 0.04 0.71 ± 0.14 0.80 ± 0.18

5 Competition-binding of typical antagonists of the nAChRs, e.g., tubocurarine and α-Bungarotoxin, have a high affinity for His-tagged AChBP, respectively IC50s of 93 nM and 2.6 nM. The cholinergic antagonist succinylcholine has a very low affinity for His-tagged AChBP (IC50 7.9 mM). Interestingly, also muscarinic receptor antagonists bind to His-tagged AChBP with relatively high affinity, e.g., the muscarinic allosteric modulator gallamine (IC50 39 nM), and the muscarinic antagonist atropine (IC50 5.3 mM). Physotigmine which is a known blocker of acetylcholinesterase and is also an antagonist of the nAChR, binds to His-tagged AChBP with an IC50 of 1.3 mM.

Finally, Bipinnatin-B was tested, a synthetic form of the coral lophotoxin on AChBP (Groebe and Abramson, J. Biol. Chem. 270 (1995), 281-286). Bipinnatin-B is a general blocker of nAChRs and is known to covalently bind to Tyr-190 of the α subunits (Abramson, J. Biol. Chem. 263 (1988), 18568-18573). His-tagged AChBP was incubated with the toxin, and the mass of the protein increased with 430.1 Da, corresponding well to the calculated mass of Bipinnatin-B of 431 Da, indicating that the toxin also binds to Tyr-184 in His-tagged AChBP.

EXAMPLE 5: Expression and purification of recombinant AChBP for crystallization

The AChBP_T1 protein from Lymnea stagnalis (AChBP) was overexpressed in Pichia pastoris GS115 strain using the AOX1 gene expression system from Invitrogen. Media and methods used for AChBP expression are also described in Invitrogen manual Pichia Expression Kit. For long term storage the transformants were grown overnight in YPD medium at 30°C.

-55

YPD or Yeast Extract Peptone Dextrose medium

1% yeast extract (Difco)

2% peptone (Difco)

2% dextrose (glucose) (Merck)

The cells were harvested and suspended in YPD medium containing 15% glycerol at final OD600 of ~50. The cells were frozen in a dry ice/ethanol bath and stored in the freezer (Revco) at ~80°C. Normally, the expression of AChBP started with plating the cells from the glycerol stock on MD plate.

MD or Minimal Dextrose Medium

10 1.34% YNB (yeast nitrogen base w/o amino-acids) (Difco)

4x10-5 % d-biotin (Sigma)

1% dextrose

For plates add 15g of agar (Difco)

The plate was stored in the incubator (Heraeus) for 3-4 days at 30°C. A single colony was picked from the plate and inoculated in 150 ml baffled flask (Nalgene) containing 25 ml of BMGY medium.

BMGY or Buffered Glycerol-complex Medium

1% yeast extract

2% peptone

20 100 mM potassium phosphate (pH 6.0) (Merck)

1.34% YNB

25

30

4x10-5 % d-biotin

1% glycerol (Merck)

The culture was placed into the shaker (New Brunswick) and left to grow overnight rotating at 250 rpm at 30°C. The following day 12.5 ml of the culture was inoculated into 225 ml of BMGY medium in a 1000 ml baffled flask. In order to increase the yield of expressed AChBP a larger number of flasks were used, usually 16. The flasks were placed in the shaker and start-cultures were rotated at 250 rpm at 30°C. After two days the start-cultures were centrifuged for 15 min at 2500 rpm (Sorvall RC3B+, rotor H-6000A) at room temperature. In order to increase the cell mass for bigger protein production, cell pellets of two start-culture flasks were pooled together and resuspended in 200 ml of BMMY medium containing 1% (w/v) casamino acids.

BMMY of Buffered Methanol-complex Medium + 1% casamino acids

1% yeast extract

35 2% peptone

100 mM potassium phosphate (pH 6.0)

1.34% YNB

-56

4x10-5 % d-biotin

5

10

15

20

25

30

35

0.5% methanol (Merck)

1% casamino acids (Difco)

The cultures were put back into the shaker (250 rpm, 30°C) and induced for the following 4 days. The concentration of methanol in the medium was kept constant by adding 1% (v/v) methanol to the cultures every 24 hours. After 4 days 100 ml of culture was harvested and the original volume of 200 ml was readjusted by adding fresh BMMY medium with 1% casamino acids. The remaining cultures were induced for another 4 days. The harvested cultures were centrifuged for 15 min at 4000 rpm (Sorvall RC3B+, rotor H-6000A) and the cell pellet was discarded. The supernatant was first filtered through a 0.22 µm filter (Millipore) to remove any remaining cells and it was concentrated using a Minitan system (Waters/Millipore) with 30kDa cutoff filter (Waters/Millipore). Both the filtration and concentration and were performed at 4°C. Finally, centrifugation at 16000 rpm was done (Sorvall RC5C, rotor SS-34) in order to remove any debris left after the first two steps. The final volume of concentrated sample was ~80 ml and it was dialyzed overnight against 2 x 5 l (20 mM Tris [pH 8.0], 150 mM NaCl and 0.02% NaN3) using 15kDa cutoff dialysis membrane (Spectra/Por) at 4°C. The dialyzed protein solution (~100 ml) was loaded onto an anion-exchange column (POROS 50 HQ, Pharmacia, column volume 8 ml). After the initial wash step of ~15 column volumes using loading buffer, a salt gradient of 30 column volumes was run from 150 mM to 1000 mM NaCl. Both solutions contained also 20 mM Tris (pH 8.0) and 0.02% NaN3. The peak of interest eluted at ~300 mM NaCl (conductivity range 16-24 mS/cm). The presence of AChBP was checked by Bio-Rad Protein Assay (Bio-Rad) and SDS-PAGE and the fractions of interested were pooled and concentrated using a Centriprep with a 30kDa cutoff membrane (Amicon). The concentrated sample (volume of 5 ml) was loaded onto a gel filtration column (Superdex 200 HR 16/60, Pharmacia, column volume 120 ml) using 20mM Tris (pH 8.0), 150 mM NaCl and 0.02% NaN3. The protein eluted starting from 60 to 71 ml with peak at ~66 ml. The final purification step of the protein was done on an anion-exchange column (MonoQ HR10/10, Pharmacia, column volume 6 ml). The protein was loaded onto the column in the same buffer as eluted from the gel filtration column. The salt gradient used for the column was the identical to the one used for the POROS 50 HQ column. The fractions in the conductivity range 25-27.5 mS/cm were pooled together and dialyzed against buffer containing 50 mM HEPES (pH 7.0) and 0.02% NaN3. The protein was concentrated up to ~20 mg/ml using a Centricon with a 30kDa cutoff membrane (Amicon). The total yield was about 2 mg purified

-57

protein per liter of expressed medium. The concentrated protein was stored at 4°C and used for crystallization experiments and biochemical characterization. N-terminal sequencing revealed the presence of EAEAYVEF residues that are part of the plC9-encoded signal sequence, before residue 2. The experimental mass was determined to be 26544 Da (MALDI), which is ~2kDa more than calculated mass based on amino-acid sequence (24649 Da). The difference is assigned to glycosylation of AChBP at position Asn66 in the mature sequence, confirmed by deglycosylation experiments with N-glycosidase F (Boehringer).

The purification of the first harvest was done separately from the full harvest. They were pooled together prior to the last purification step (anion-exchange chromatography step on MonoQ column). All above mentioned chromatography columns were mounted on an FPLC system (Pharmacia) controlled by the UNICORN system (Pharmacia). All solutions used in the FPLC system were prepared with MilliQ UF+ water, filtered through 0.22 µm filter (Millipore) and degassed.

15

20

25

30

35

10

EXAMPLE 6: Crystallization of the AChBP

All the crystallization experiments were done by vapor diffusion technique in a hanging drop mode using 12 well tray (Nelipak) and siliconized cover slides (Hampton Research). Trays were placed in a sandwich box (Semadeni) and stored at 19°C temperature conditioned room. The initial crystallization attempts were performed using Hampton Crystal Screen I and II (Hampton Research). Drops contained 2 µl of protein (10 mg/ml in 50 mM HEPES [pH 7.0] and 0.02% NaN₃) and 2 µl of reservoir solution. From the first screen it became clear that AChBP makes crystalline precipitate in the presence of CaCl2 salt. A more detailed screen was made which produced crystals suitable for X-ray analysis. The AChBP crystals appeared in the following conditions: 9-11% (w/v) PEG 4000 (Hampton Research), 100 mM HEPES (pH 7.0), 50-200 mM CaCl₂ x 6H₂O and 0.02% NaN₃ or or PEG MME 550 10-18% in the same conditions, with 0.3 mM ZnAcetate as additive. Depending on the batch of the protein used and the CaCl2 concentration three different crystal forms were found: orthorhombic, tetragonal and monoclinic. Both orthorhombic and monoclinic crystal forms are frequently twinned. Orthorhombic rodlike crystals appeared immediately upon setting up the crystallization experiments (in between first few hours) under high [CaCl2]. The size of the crystals varied from 0.05x0.05x0.15 to 0.25x0.25x1.0 mm. The crystals diffract X-ray up to 3 Å resolution and show high degree of mosaicity (~05-1.2°). They have the symmetry of space group $P2_12_12_1$ with cell constants of a= 120.62Å, b=137.01Å, c=161.54Å with 2 pentamer molecules per asymmetric unit. Tetragonal crystals, squared in shape,

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-58

grew at lower $CaCl_2$ concentration, reaching 0.2x0.3x0.35 mm in size. The maximal resolution obtained was 2.7 Å with a lower mosaicity (0.5°) . They belong to space group $P4_22_12$ space group with cell dimensions of a=b=141.66Å, c=120.83Å with one pentamer molecule per asymmetric unit. The exact crystallization condition for the tetragonal crystal which was used for refinement of the crystal structure: 11.5% (w/v) PEG 4000, 100 mM HEPES (pH 7.0), 150 mM CaCl₂ and 0.02% NaN₃. The third crystal form, monoclinic $P2_1$, is very similar in morphology to the orthorhombic crystals with cell dimensions of a=121.1Å, b=162.1Å, c=139.4Å, $\beta=90.13^{\circ}$, containing 4 pentamers per asymmetric unit. This crystals were gave lower resolution data (~3.3Å resolution). All three crystal forms were used in the structure determination of AChBP.

The resolution limit of diffraction depended very much on the size of the crystals. And the largest crystals diffracted weakly to ~4Å resolution when exposed to a conventional rotating anode X-ray source. Therefore, the use of synchrotron radiation was critical for the structure determination. The crystals had to be cryo-protected in order to slow down the damage caused by high intensity synchrotron radiation. The cryo-protection of the AChBP crystal was done in multiple steps. The first steps included the stabilization of crystal by adding the 2 µl of mother liquor (equilibrated reservoir solution) to the drop with the crystal. After 5 minutes 3 µl of stabilizing solution was added to the drop. Normally, the stabilizing solution contained slightly higher concentrations (1-5%) of the components of the original crystallization buffer. As protectant glycerol (Merck) was added, increasing the concentration stepwise from 0% to 30% (v/v). For example, the starting solution contained 15% PEG 4000, 100 mM HEPES (pH 7.0), 150 mM CaCl₂ and 0.02% NaN₃ and the final solution contained 30% (v/v) glycerol in addition to the components just mentioned. The AChBP crystals do not tolerate drastic increase in the glycerol concentrations therefore a gentle but more time consuming approach has to be adopted. The solution around the crystal has to be stepwise exchanged (usually 5% increase of glycerol concentrations) allowing crystals to equilibrate for at least 5 minutes in each glycerol concentration. Once the crystals were equilibrated in stabilizing solution with 30% glycerol they were flash-cooled in liquid nitrogen or in the cryo-stream. In all three space groups AChBP forms a decamer structure with perfect 52 symmetry, where two pentamers contact each other through a calcium-binding site, at the 'top' of the a1 helix. This binding site (Asp2 and Asp5 from two monomers) is not conserved in the LGIC family. In the tetragonal space group the 2-fold of the a crystallographic two-fold, which leads with coincides decamer

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-59

pseudocentrosymmetric behavior of the phases at low resolution. In solution the AChBP protein acts as pentamer.

Those of skill in the art will appreciate that the aforesaid crystallization conditions can be varied. Such variations may be used alone or in combination, and include final protein (optionally in complex with a ligand) concentrations between 1 mg/ml and 30 mg/ml; all combinations of AChPB/ligand to precipitant ratios; use of citrate concentrations between 0 mM and 200 mM; DTT concentrations between 0 mM and 10 mM; and any concentration of beta-mercaptoethanol; pH ranges between 5.5 and 9.5; PEG concentrations between 5% and 25% (w/v); PEG weights between 2000 and 8000; HEPES concentrations between 5 and 500 mM; use of TRIS or other solutions instead of HEPES, and any concentration or type of detergent; any other type of precipitating agent; any other buffer; any temperature between –50 °C and 30 °C; and crystallization of AChBP or complexes thereof by batch, liquid bridge, or dialysis method using these conditions or variations thereof.

EXAMPLE 7: Structure determination

The crystal structure was determined using the multiwave anomalous dispersion (MAD) technique on a Pb derivative, but non-crystallographic symmetry (NCS) averaging was necessary to obtain interpretable electron density. Collection of native data and heavy-atom derivatives were carried out at the synchrotron beam-lines in Grenoble (ESRF/BM14 and ID14) and Hamburg (DESY/BW7A, BW7B and X11). The AChBP orthorhombic crystal was soaked in stabilizing solution containing 5 mM trimethylleadacetate (MePb) for 5 days. Data sets were collected at four different wavelengths (0.9492Å, 0.8610Å, 0.9507Å and 0.9499Å) and data were integrated and reduced using DENZO/SCALEPACK (Otwinowski and Minor (1997) Processing of X-ray diffraction data collected in oscillation mode. In Methods in Enzymology, Volume 276: Macromolecular Crystallography, part A. C.W. Carter and R.M. Sweet, eds. (New York: Academic Press), pp. 307-326). The program SOLVE (Terwilliger (1997) SOLVE: An automated structure solution for MAD and MIR. Edition 1.16) found 5 Pb sites which were situated on the interface between two pentamers. The Pb parameters were refined and phases calculated with SHARP (La Fortelle et al. (1997) Advances in MIR and MAD phasing: Maximum-likelihood refinement in a graphical environment, with SHARP. Proceedings of the CCP4 study weekend). Mean figure of merit (FOM) value for 4 wavelengths was 0.45. Search and optimization of 5-fold NCS operators were done using programs NCS6D and IMP (Kleywegt and Jones (1999) Software for handling macromolecular envelopes. Acta

15

20

25

30

35

-60

Crystallo., D55, 941-944). 10-fold averaging using refined NCS operators in conjunction with density modification by DM (Cowtan (1994) DM: An automated procedure for phase improvement by density modification. In Joint CCP4 and ESF-EACBM Newsletter on Protein Crystallography 31, 34-38) yielded an interpretable electron density map. However, some parts of the pentamers were still not clearly defined. Therefore, a second MAD experiment was performed on the monoclinic crystals soaked in 10 mM MePb for 5 days. Data were collected for only two wavelengths, at the Pb peak (0.9479Å) and remote (0.9498Å) wavelength. The processing of the two collected data sets was done with MOSFLM (Leslie (1992) Recent changes to the MOSFLM package for processing film and image plate data. In Joint CCP4 and ESF-EACBM Newsletter on Protein Crystallography, Number 26) and data were scaled with SCALA (CCP4. The CCP4 suite: programs for protein crystallography. Acta Crystallog. D50, 760-763). 10 Pb sites were identified with Solve. The Pb parameters were refined and phases calculated with SHARP in single anomalous dispersion (SAD) mode using data collected at the Pb absorption peak The NCS operators needed for 20-fold averaging were found by NCS6D and improved with IMP. 20-fold averaging and density modification by program DM further improved electron density. The initial model tracing and sequence assignment were done based on the 20-fold averaged electron density with program O (Jones et al., 1991). However, parts of the molecules were not clearly defined. The electron density was further improved doing multi-crystal averaging with DMMULTI (Cowtan, 1994) using amplitudes of tetragonal, orthorhombic and native data sets and experimental phases of the orthorhombic and monoclinic MAD experiments. Initially missing parts became clearly defined and a complete model could be built. The initial atomic model was refined with the program CNS (Brünger et al. (1998) Acta Crystallogr. D 54, 905-921) against a maximum-likelihood target without experimental phases contribution using tetragonal native data which extend to 2.7Å resolution. Refinement included five-fold NCS restraints, an overall anisotropic B factor and bulk solvent correction. The five-fold NCS restraints were released for the parts of the pentamer that clearly do not follow the five-fold symmetry. The current model contains one pentamer of AChBP consisting of 1035 residues, 14 well-ordered solvent molecules, 5 Ca2+ ions, 5 Cl- ions and 5 Hepes molecules, well-ordered solvent molecules and 5 HEPES molecules. The following residues are not well defined in the electron density: -8-0 (part of α-mating S. cerevisiae signal sequence not native to AChBP EAEAYVEF; SEQ ID No. 21), 125-135, 155-165, 186-191 and 206-210.

10

15

-61

Electron density is detectable in the ligand-binding site of AChBP. It is presumed that a HEPES molecule could account for this extra electron density based on its chemical properties. HEPES or N-2-Hydroxyethylpiperazine-N'-2-ethanesulfonic acid contains a quaternary ammonium ion similar to ligand such as acetylcholine (ACh) and d-tubocurarine. It has been proposed that the binding of ACh would be mediated by cation- π interaction involving N⁺ and π -systems of aromatic residues present in the binding site of nicotinic acetylcholine receptor. Without intending to be bound by theory it is suggested in accordance with the observation of the present invention that the observed HEPES molecule mimics ligand binding analogous to the binding of natural ligands like ACh in the ligand-binding site.

EXAMPLE 8: More detailed description of the structure determined in Example 7 As described in the previous example, the crystal structure of AChBP was solved using weak Pb MAD data in two crystal forms. The electron density map was improved substantially by cross-crystal averaging of three crystal forms with 20, 10 and 5 copies of the monomer in the asymmetric unit respectively (Table 3).

Table 1: Data collection statistics

	Data set	<u>λ₁ peak</u>	λ ₂ remote	<u>λ₃ infl.</u>	λ_1 peak	λ_2 infl.	<u>Native</u>
20	Space group	P2 ₁ 2 ₁ 2 ₁			<i>P</i> 2 ₁		P4 ₂ 2 ₁ 2
	Resol. (Å)	3.3/3.4-3.3	.3/3.4-3.3		3.0/3.1-3.0		2.7/2.8-2.7
	λ (Å)	0.9492	0.8610	0.9507	0.9479	0.9498	0.943
	Compl. (%)	99.7/99.7	99.6/99.6	99.7/99.7	99.9/99.9	99.5/99.5	97.8/96.5
	Mosaicity (°)	0.62			0.43		0.78
25	Redundancy	3.7/3.8	3.8/3.9	3.7/3.8	3.5/2.2	3.2/2.0	6.5
	R _{merge} (%)	7.7/46.8	7.8/45.2	8.3/55.0	5.9/26.1	6.0/32.9	5.9/67.4
	Vol	8.7/1.6	8.4/1.7	8.3/1.4	7.7/2.7	6.8/1.5	27.4/2.3

			-62		
Phasing	ISO/ANO	ISO/ANO	ISO/ANO	ISO/ANO	ISO/ANO
R _{cullis} (%)	0.74/0.89	n.a./0.92	0.54/0.94	n.a./0.74	0.66/0.77
Phasing power	0.57/1.2	n.a./1.06	2.3/0.91	n.a./1.1	0.37/1.22
FOM (overall)	0.45			0.28	

5

10

15

20

25

30

35

The structure was refined at 2.7 Å in space group P42212, with one AChBP pentamer in the asymmetric unit. Thus, native data (X11) were collected and the Pb-1 data sets (BW7A) at the EMBL/DESY synchrotron in Hamburg and the Pb-2 data sets (BM14) at the ESRF, Grenoble (Table 3). Data were processed with DENZO/SCALEPACK (Otwinowski & Minor, Methods Enzymol. 276, 307-326 1997) (native) or MOSFLM (Leslie, Acta Crystallogr. D. Biol. Crystallogr. 55, 1696-1702, 1999)/SCALA (CCP4) (Pb-1, Pb-2). The Pb sites, located at the interface of two pentamers, were found for both MAD sets by SOLVE (Terwilliger, Acta Crystallogr. 55, 849-861, 1999) and heavy atom parameters were optimized with SHARP (La Fortelle et al., Methods Enzymol. 276, 472-494, 1997). NCS operators were found and refined with NCS6D and IMP (Kleywegt and Jones, SERC Daresbury Laboratory, Warrington, pp. 59-66, 1994). DM-multi (Cowtan, Joint CCP4 and ESF-EACBM Newsletter on Protein Crystallography, 31, 34-38, 1994) multi-crystal averaging used amplitudes of monoclinic, orthorhombic and native (tetragonal) data sets and experimental phases of the orthorhombic and monoclinic MAD experiments. The model was built in O (Jones et al., Acta Crystallogr. A47, 110-119, 1991) and refined with the program CNS (Brünger et al., Acta Crystallogr. D54, 905-921, 1998), against the tetragonal data to 2.7 Å resolution. Refinement included partial 5-fold NCS restraints, an overall anisotropic B factor and bulk solvent correction. The unusual double cysteine Cys187-Cys188 formed a clear disulfide bridge. Because of the limited resolution it was refined with standard parameters. The final model contains 1025 residues of AChBP pentamer, 5 HEPES molecules, 10 Ca2+ ions and 15 water molecules. The entire AChBP pentamer is well ordered, except for the N-terminal 7 residues (part of the signal sequence) and the last five C-terminal residues. In addition, the HEPES, the loop region 155-160 and the sugar residues attached to residue Asn66 are not well resolved in the electron density. R.m.s deviations from ideal geometry for bond distances and angles are 0.01 Å and 1.6°, respectively. The sequence alignment was calculated by CLUSTALX (Thompson et al., Nucleic. Acids. Res. 25, 4876-4882,

-63

1997) and the corresponding figure with Espript (Gouet et al., Bioinformatics. 15, 305-308, 1999). Figures 2-5 were done using programs MOLSCRIPT (Kraulis, P.J., J. Appl. Cryst. 24, 946-950, 1991), BOBSCRIPT (Esnouf, Acta Crystallogr. D55, 938-940, 1999) and RASTER3D (Merritt and Bacon, Methods Enzymol. 277, 505-524, 1997). Refinement took place with partial five-fold NCS restraints, resulting in an R-factor of 26.4% (R_{tree} = 30%).

The AChBP pentamer.

5

10

15

The AChBP homopentamer, when viewed along the five-fold axis, resembles a windmill toy, with petal-like monomers (Fig. 6a). When viewed perpendicular to the five-fold axis it has a disc-like appearance (Fig. 6b). The overall proportions of the pentamer are ~80x80x62 Å, and the diameter of the central hole is ~18 Å. These dimensions are in good agreement with the *Torpedo* nAChR N-terminal domain EM data (Miyazawa et al., J. Mol. Biol. 288, 765-786, 1999). The only subunit contacts in the AChBP pentamer are dimer interfaces, of which each monomer has two, one called the plus side and one called the minus side. We refer to the A (plus)-B (minus) interface, as example for the five equivalent interfaces AB, BC, CD, DE and EA (Fig 6).

20 The AChBP monomer:

Each AChBP monomer is a single domain protein, asymmetric in shape, with a size of ~50x21x27 Å (Fig. 12a). It consists of an N-terminal β -helix, two short 3_{10} helices and a core of 10 β -strands forming a β -sandwich. The order of β -strands conforms to a modified immunoglobulin (Ig) topology (Fig. 12b) with an extra β -hairpin (f'-f") and an extra strand (b') (Bork et al., J. Mol. Biol. 242, 309-320, 1994). These additional strands introduce two so-called "Greek key" folding motifs. The Ig-based structure prediction (Le Novère et al., 1999; Corringer et al., Biophys. J. 76, 2329-2345, 1999) agrees well with the AChBP structure, although location of the binding site was missed due to the presence of extra β -strands (Fig. 12b). Compared to the classical Ig-fold, the AChBP β -strands are considerably twisted, with the β -sheets rotated against each other, resulting in two separate hydrophobic cores. Thus the three-dimensional fold does not resemble other Ig-like proteins and comparison to the protein database (Holm and Sander, Nucleic. Acids. Res. 25, 231-234, 1997) did not result in a significant match to any known structure.

30

15

20

25

WO 01/58951 PCT/EP01/01457

-64

Positioning of functional regions:

Couple of regions that are important to receptor function can be localized in the AChBP structure. In muscle type nAChRs the main immunogenic region (MIR), comprising residues α_167 - α_176 , acts as an epitope in the autoimmune disease myasthenia gravis (Tzartos et al., Mol. Neurobiol. 5, 1-29, 1991). Although the MIRrelated region in AChBP (residues 65-72) shows no sequence homology to the α₁subunit, its location in loop L3 at the top of the pentamer in a highly accessible position agrees well with the expected accessibility for this region. It also fits with EM studies that located the MIR at the distal end of the receptor relative to the membrane (Beroukhim and Unwin, Neuron 15, 323-331, 1995). On each AChBP monomer, a large cavity that is accessible from the central pore of the pentameric ring can be seen. The cavity is framed at the entrance by $\beta\mbox{-strands}$ (β 3, β 4, β 5 and β 5') (Fig 12a) and is uncharged, mainly hydrophobic, in character. This region probably corresponds to the tunnel framed by twisted β-strands that was observed in the α_1 -subunit of Torpedo receptor at 4.6 Å resolution (Miyazawa et al., J. Mol. Biol. 288, 765-786, 1999). However, this cavity is not in contact with another large pocket observed at each interface between subunits. These latter pockets are

J. Mol. Biol. 288, 765-786, 1999). However, this cavity is not in contact with another large pocket observed at each interface between subunits. These latter pockets are lined by residues shown to be involved in ligand binding in nAChR (Arias, Neurochem. Int. 36, 595-645, 2000; Corringer et al., Annu. Rev. Pharmacol. Toxicol. 40, 431-458, 2000). They are buried from the solvent, and located close to the outside of the pentameric ring. When viewed perpendicular to the five-fold axis they are roughly equatorially positioned, ~30 Å away from the C-termini (Fig. 6b), conforming to the expected location of the *Torpedo* receptor ligand-binding site, as determined by labeling (Fernando Valenzuela et al., Biophys. J. 66, 674-682, 1994)

The ligand-binding site:

30 Each ligand-binding site is found in a cleft formed by a series of loops from the principal face of one subunit and a series of β-strands from the complementary face of an adjacent subunit. It is a large cavity buried by a series of loops from the principal side and by a β-strands from the complementary side (Fig. 13). The principal side on the plus side of the AB interface consists of residues coming from 'loop A' (TyrA89), 'loop B' (TrpA143, A145) and 'loop C' (TyrA185, the double cysteine A187-A188, and TyrA192) (Fig 13c). The complementary part of this binding

and EM studies (Unwin, J. Mol. Biol. 229, 1101-1124, 1993).

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-65

site is contributed by monomer B and made of 'loop D' (TrpB53, GlnB55), 'loop E' (ArgB104, ValB106, LeuB112 and MetB114) and 'loop F' (TyrB164) (Fig 13d). In this pocket four of the aromatic residues form the bottom half of the cavity (TyrA89, TyrA185, TyrB164 and TrpB53). The pocket walls are formed by the TyrA192, TrpA143, main chain of A145 Met B114, the side-chain of GlnB55 and the double cysteine (CysA187-CysA188). The hydrophobic parts of ArgB104, ValB106 and LeuB112 form the top of the pocket (Fig 13a).

All residues in the pocket had been successfully identified by photoaffinity labeling and mutagenesis studies (Arias, Neurochem. Int. 36, 595-645, 2000; Corringer et al., Annu. Rev. Pharmacol. Toxicol. 40, 2000). Although the side chain of HisA145 is pointing away from the cavity, its main chain is involved. One residue identified by labeling studies, TrpA82 (α₁Trp86) (Galzi et al., J. Biol. Chem. 265, 10430-10437, 1990; Dennis et al., Biochemistry 27, 2346-2357, 1988) is involved in hydrophobic core formation and located far from the pocket, thus not participating in ligand binding. Otherwise, the AChBP ligand-binding site confirms the available blochemical

The structure, however, shows for the first time how these residues are positioned with respect to each other and therefore provide a valuable tool for drug design as described in the above description of the present invention.

and mutational data on nAChR completely.

All observed residues are conserved between known nicotinic ligand-binding subunits except the 'loop F' TyrB164 residue. The 'loop F' region has an unusual conformation, but since it is relatively weakly resolved, its precise analysis is difficult. The 'loop F' region is stabilized in the structure by a calcium binding site formed by AspB161, AspB175 and the main chain of B176. This Ca2+ ion is structurally important for TyrB164 orientation and could therefore be important for proper ligand binding. The present findings are supported by labeling studies on muscle/Torpedo subunits showing that residues homologous to AspB161, γAsp174/δAsp180 play a role in ligand binding (Czajkowski et al., Proc. Natl. Acad. Sci. U.S.A. 90, 6285-6289, 1993; Czajkowski and Karlin, J. Biol. Chem. 270, 3160-3164, 1995; Martin et al., J. Biol. Chem. 271, 13497-13503, 1996). Additionally, calcium binding sites that enhance the response to agonist binding have been identified in the homologous region (residue range 161-172) of neuronal α₇ receptor (Galzi et al., EMBO J. 15, 5824-5832, 1996). The 'loop F' region has low sequence conservation in the nicotinic family (Fig. 11) and in other superfamily members it may well have a different conformation, even to the extent of forming a β-strand that connects the two sheets

-66

into a β -barrel. Such changes could well lead to variations in affinity, *e.g.* by changing the size of the ligand-binding site or its access route.

The most likely access routes to the ligand binding sites are from above or below the double-cysteine-containing 'loop C' (Fig. 13a). This region buries the pocket from the solvent and therefore prevents access from the outside. Access from the central pore has been suggested in the literature (Miyazawa, J. Mol. Biol. 288, 765-786, 1999), but this would require major structural rearrangements at the interface, which makes it less likely.

10

15

20

5

Ligand binding:

Surprisingly, features of bulky electron density were found that stacked onto Trp143 in each ligand-binding site in the experimental cross-crystal averaged electron density (Fig 13b). Upon consideration we have assigned this to a HEPES (N-2-Hydroxyethylpiperazine-N'-2-ethanesulfonic acid) buffer molecule, that contains a positively charged quaternary ammonium group and therefore has some similarity to known nicotinic receptor ligands. Its EC50 is 100 mM, indicating that its binding under crystallization conditions (100-150 mM) is possible. Although HEPES molecule does not make any specific contacts with the protein, it stacks with its quaternary ammonium onto Trp143, making cation- π interactions as expected for nicotinic agonists (Dougherty, Science 271, 163-168, 1996) (Fig. 13b). However, due to limited resolution of the present data and probable low occupancy, the precise orientation of the HEPES molecule should be taken with some degree of reservation.

It has been suggested (Changeux and Edelstein, Neuron 21, 959-980, 1998) that the ligand-binding site of nAChRs could be similar to that of acetylcholinesterase (AChE). Although the size of the binding site is roughly similar in AChBP and AChE, the observed arrangement of aromatic residues is quite different. However, the stacking of the quaternary ammonium of HEPES, as far as it has been refined in the current AChBP structure, is similar to that of the quaternary ammonium of the decamezonium in AChE on the Trp84 residue (Harel et al., Proc. Natl. Acad. Sci. U.S.A. 90, 9031-9035, 1993).

Subunit arrangement:

From the location of the ligand-binding site conclusions can be drawn about the relative arrangement of subunits in the *Torpedo* and muscle receptors. It has been suggested that the $\alpha_1\gamma$ and $\alpha_1\delta$ interfaces occur in a clockwise $\alpha_1\gamma\alpha_1\delta\beta_1$ arrangement

-67

when looking towards the membrane (Machold et al., Eur. J. Biochem. 234, 427-430, 1995). Such a clockwise arrangement disagrees with the structure determined in accordance with the present invention, because the relative arrangement of the principal binding site and its complementary partner is anticlockwise when looking towards the 'bottom' (membrane) side of the pentamer (Fig. 6).

Pentamer interface:

5

10

15

20

25

The subunit interface consists on the plus side entirely of loop regions (L1, L2, L4, L5, L7, L8 and L10), whereas the minus side mostly presents secondary structure elements to the interface (α 1, β 1, β 2, β 3, β 5, β 6 and L9) (Fig. 14). Several residues are important for both ligand-binding and pentamer formation. The interface buries a considerably surface area (2700 Å²), with a mainly uncharged character including only a single bifurcated salt bridge (GluA149-ArgB3 and ArgB104). Most intriguing about the interface residues is the lack of conservation of these particular residues in the entire superfamily, not only with AChBP, but also amongst each other (Fig. 11). These changes involve major changes in character, including changes from hydrophobic to charged. Even when a residue is conserved in any particular subunit, its expected counterpart is missing (either in the same subunit, as in the α_{7} homopentamers, or in contacts such as muscle $\alpha_1\delta$ or $\alpha_1\gamma$ or neuronal $\alpha_4\beta_2$) with the sole exception of the ligand-binding site. The high level of structural conservation however, determines involvement of the same topological regions in these contacts in all family members (Fig 14b). This indicates that shape complementarity must play a major role in determining the conservation of the pentamer structure. It also indicates that different combinations of subunits will have different interfaces, creating variations in the precise allosteric contacts and movements in the various subclasses of these ion channels.

Ligand-gated ion channels:

The lack of conservation of the interface residues seems a general feature in the superfamily of LGICs, as the residues that form the interface are among the least conserved regions of the domains (Fig. 11). Apparently pentamer formation does not impose very stringent evolutionary requirements in this case. However, there is clear sequence conservation within the superfamily (Fig. 11) and it is interesting to analyze this in the light of the structure.

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-68

In the AChBP monomer structure the conserved hydrophobic residues can be grouped into three clusters (Fig. 15). In AChBP, as in other proteins with Ig-like fold, the packing of the β-sheets is promoted mainly by hydrophobic and to a lesser extent by electrostatic interactions. The first cluster is involved in packing of the N-terminal helix a1 against the main framework of the monomer and it involves residues 6, 10, 63, 65, 71, 81, 105 and 111. The second cluster, comprising residues 20, 27, 29, 31, 58, 82, 84, 86, 140, 150, 152 and 195, is situated in the upper half of the β-core region. The third cluster, including residues 33, 35, 38, 41, 48, 52, 125, 138, 171, 173, 199 and 201, is located at the lower end of the structure (Fig 15). The only nonhydrophobic residues that are highly conserved in the superfamily are Asp60, Asp85, Asn90 and Gly109. Asp60 and Gly109 are involved stabilizing the turns of a Greek key motif connecting strands β3, β5, β6 and β2, where Asp60 stabilizes the Nterminus of a small 310 helix and Gly109 enables tight turn formation. Conserved residues Asp85 and Asn90 are involved in packing of the β-sheets. Asp85 forms hydrogen bonds to the highly conserved Ser142 and Thr144 and residue Asn90 brings together the main-chain oxygens of Ser122 and Arg137, enabling disulfide bond formation of the nearby absolutely conserved disulfide bond (123-136). This disulphide bond is topologically equivalent to so-called 'tyrosine cornerstone' (Hemmingsen et al., Protein Sci. 3, 1927-1937, 1994), which links the two β-sheets together in Ig-like proteins. This explains why in the Torpedo receptor the Cys128-Cys142 bond is important for both preservation of subunit conformational stability (Mishina et al., Nature 313, 364-369, 1985) and complete nAChR assembly (Green & Wanamaker, J. Neurosci. 18, 5555-5564, 1998). Since the observed overall structural conservation is high, it is clear that all LGIC N-terminal domains will have the same three-dimensional structure.

In contrast to the above residues, the Cys-loop is a highly conserved hydrophobic region in the LGIC family but presents a totally different character in AChBP (Fig. 11).

In AChBP, this loop is hydrophilic and is found at the bottom (membrane) side of the protein, at the dimer interface. This location and its hydrophobicity in the LGIC family implies that this loop could interact with the membrane or with the transmembrane region of the receptors, functions that are absent in AChBP.

Since all ligand gated ion channels have intrinsically the same function, opening of a membrane pore, it is likely that the conserved regions of the protein determine this function. That also indicates that it is unlikely that the interface of the pentamer has a major role in opening the channel. It is possible that the conserved Cys-loop is

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-69

directly involved in transmitting this kind of information to the membrane part of the LGICs. Another option is that large structural changes in the β -sheet regions play a role in opening the channel. Indeed, the movement observed at 9 Å for *Torpedo* nAChR upon agonist binding (Unwin, Nature 373, 37-43, 1995), fits well with such a suggestion. In accordance with the present invention a twisted β -sandwich would be observed, with two distinct hydrophobic cores and it is entirely possible that these cores move with respect to each other upon ligand binding. The effect of such movements will then be modulated by the varying subunit interfaces in the different subtypes of the receptor, allowing intricate specificity in the neuronal signal transmission.

EXAMPLE 9: Ligand-binding crystallization studies

AChBP was cocrystallized in complex with α-bungarotoxin (αBTX, Sigma). Prior to the crystallization experiments the stability of the complex has been investigated. Using gel-filtration chromatography (Superdex 200 HR 10/30, Pharmacia, column volume 24 ml) it has been found that it is possible to purify stable complex between AChBP and αBTX. The gel-filtration run was performed using 20 mM Tris (pH 8.0), 150 mM NaCl and 0.02% NaN₃. The stability of the complex was also confirmed with native PAGE. The crystallization experiments were done based on the same set of conditions found to work for AChBP alone; see Example 6. A small screen was set up with different precipitant concentrations and various AChBP:α BTX concentrations. Tiny crystals appeared in the conditions containing 10-12% PEG 4000, 100 mM HEPES (pH 7.0), 20-80 mM CaCl₂ and 0.02% NaN₃. The best looking crystals grew under above mentioned conditions when AChBP: ⟨BTX were mixed in 1:10 molar ratio. In order to check if complex indeed crystallized, crystals were thoroughly washed, dissolved in denaturing buffer and checked on SDS-PAGE that clearly showed that they contained both proteins.

In addition, a number of small ligands were bound to AChBP in soaking experiments. These include: B-bippinatin (a synthetic analog of lophotoxin), acetylcholine (ACh, Slgma), d-tubocurarine chloride (Sigma), carbamylcholine chloride (CCh, Sigma), galanthamine hydrobromide (Sigma), epibatidine (Sigma) and nicotine (Sigma). The soaking solutions were made of stabilizing solutions (see Example 6) and together with dissolved ligands (ligands were normally dissolved in 20 mM HEPES [pH 7.0]). The ligand concentrations used were dependent on its binding constants, as determined by ligand-binding studies. The soaking times were different depending on the ligand used. After the soaking step the crystals were flash-cooled in liquid nitrogen.

10

15

20

25

30

35

WO 01/58951 PCT/EP01/01457

-70

EXAMPLE 10: Generating human alpha7 nAChR / AChBP chimeras

The chimeric proteins of nAChR subunits and AChBP can be used as tools in the development of novel, nAChR subtype specific ligands. As a first step in developing these tools chimeric proteins have been designed and constructed in which part(s) of the human alpha7 nAChR were grafted into AChBP. Previous studies on the molecular determinants of ligand-binding by the alpha7 nAChR have identified three amino acid domains that compose the primary part of the ligand-binding site, further referred to as "loops A, B, and C". Within each of the three loops amino acid residues are present that are thought to directly interact with the ligand. Based on sequence conservation of the nAChR and AChBP the three possible ligand-binding loops of AChBP have been pin-pointed in accordance with the present invention as follows: loop A, Trp-101 -> Tyr-108; loop B, Trp-162 -> His-164; loop C, Tyr-204 -> Tyr-211. The chimeric proteins that were constructed replace either one (A, B or C) or multiple (A&B, A&C, B&C and A&B&C) of the ligand-binding loops of AChBP with the corresponding human alpha7 nAChR sequence.

The loop-A domain of AChBP was replaced by the corresponding domain of the human alpha7 nAChR using a two-step polymerase chain reaction (PCR). In the first step two separate PCR amplifications (35 cycles: 94 ºC;30 sec., 58 ºC; 30 sec and 72 °C; 60 sec.) yielded two halves of the chimera construct. AChBP cDNA (wild type) was used as template, and outer primers located either just before the start codon (gcgctcgagaaaagagaggctgaagctttggaccgggcagacatctt; SEQ ID No. 17) or just before the stop codon (cgcgaattcaagaatttcggagcgtccctt; SEQ ID No. 18) were each used in combination with two internal primers gtggaaaccagacattctcctctacaacgccatctcgaaacc (SEQ ID No. 19) and gaggagaatgtctggtttccacaaagagcttattggcac (SEQ ID No. 20), respectively. The internal primers contained a 5'-tag-sequence that encoded for the introduced alpha7 nAChR domain. As such the two generated chimeric PCR products share a common tag containing a part of the alpha7 nAChR subunit. In the second step, the two PCR products from the first round were pooled and, in the absence of primers, went through 5 rounds of PCR amplification (94 °C; 30 sec., 54 °C; 3 mm. and 72 °C; 90 sec.). This allowed the two halves of the chimera to anneal to each other at the common alpha7 nAChR tag. The subsequent addition of the two outer primers and another 35 cycles of 25 PCR amplification (94 °C; 30 sec., 58 °C; 30 sec. and 72 °C; 90 sec.) yielded the final chimera construct. All PCR amplifications were hot-started and performed using PFU DNA-polymerase (Invitrogen). The loop-A AChBP/alpha7 chimera was cloned, using Xhol/EcoRI restriction sites in the outer primers, into the His-tag containing yeast expression

25

WO 01/58951 PCT/EP01/01457

-71

vector pPIC9 (Invitrogen). Validation of the construct was achieved by DNA sequencing. Expression of the chimera construct was achieved according to the Pichia pastoris protein expression protocol of Invitrogen.

As described in the examples and the description, the present invention provides 5 water-soluble ligand-binding proteins derived from molluscs and analogs of ligandgated ion channels, crystals thereof and their use for screening ligands of ligandgated ion channels. In particular, ligand-binding proteins have been identified that are capable of forming multimers and are amenable to crystallization. The crystall structure of one these proteins, an acetylcholine binding protein (AChBP) is provided, 10 which can be used to generate 3D models of the extracellular ligand-binding domain of ligand-gated ion channels and thus for screening of drugs that act on these ion channels. Furthermore, chimeric proteins are provided that are capable of binding a ligand of a ligand-gated receptor, and comprising at least the amino acids of the AChBP determining solubility of the AChBP, in the same positions as in the AChBP, 15 and furthermore comprising amino acids determining binding to said ligand. It will be clear that the invention may be practiced otherwise than as particularly

described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

The entire displayure of each document cited (including patents, patent applications)

The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Description, and Examples is hereby incorporated herein by reference. Moreover, the sequence listing is herein incorporated by reference.

PCT/EP01/01457

-72 **Table 1**

	REMARK	Writte	en by	0 v	ers	ion 7.0	.1				
	CRYST1	141.	660	141.6	660	120.8	70 90.00	90.00	90.00		
5	ORIGX1		1.000	000	0.	000000	0.000000	ס	0.00000		•
	ORIGX2		0.000	000	1.	000000	0.00000	כ	0.00000		
	ORIGX3		0.000	000	0.	000000	1.000000	D	0.00000		
	SCALE1		0.007	059	Ο.	000000	0.00000	0	0.00000		
	SCALE2	. •	0.000	000	0.	007059	0.00000	0	0.00000		
10	SCALE3		0.000	000	0.	000000	0.00827	3	0.00000		
	MOTA	1	СВ	PHE A	A	1	65.468	25.127	1.161	1.00 73.24	6
	ATOM	2	CG	PHE 2	Α	1	64.224	24.803	0.370	1.00 76.49	6
	ATOM	3		PHE 2		1	63.433	25.819	-0.178	1.00 77.52	6
	ATOM	4		PHE 2		1	63.798	23.471	0.244	1.00 78.15	6
15	ATOM	5	CE1	PHE 3	Α	1	62.224	25.522	-0.840	1.00 79.11	6
	ATOM	6		PHE .		1	62.590	23.148	-0.412	1.00 79.82	6
	ATOM	7	CZ	PHE .		1	61.797	24.179	-0.958	1.00 79.89	6
	ATOM	8	C	PHE .		1	66.638	27.146	1.923	1.00 69.89	6
	ATOM	9	Ō	PHE		1	67.034	26.519	2.903	1.00 70.26	8
20	ATOM	10	N	PHE		1	67.407	25.990	-0.118	1.00 71.31	7
	ATOM	11	CA	PHE		1	66.214	26.375	0.689	1.00 70.93	6
	ATOM	12	N	ASP		2	66.562	28.478	1.909	1.00 68.78	7
	ATOM	13	CA	ASP		2	66.958	29.233	3.105	1.00 68.57	6
	ATOM	14	CB	ASP		2	67.577	30.615	2.739	1.00 69.98	6
25	ATOM	15	CG	ASP		2	66.639	31.523	1.914	1.00 73.55	6
	MOTA	16		ASP		2	67.059	32.068	0.844	1.00 73.75	8
	ATOM	17		ASP		2	65.485	31.714	2.349	1.00 75.27	8
	MOTA	18	C	ASP		2	65.794	29.374	4.102	1.00 67.66	6
	ATOM	19	Õ	ASP		2	64.622	29.273	3.719	1.00 68.25	8
30	ATOM	20	N	ARG		3	66.126	29.560	5.386	1.00 65.60	7
00	ATOM	21	CA	ARG		3	65.131	29.703	6.453	1.00 60.77	6
	ATOM	22	CB	ARG		3	. 65.765	30.222	7.737	1.00 60.30	6
	MOTA	23	CG	ARG		3	66.393	29.174	8.604	1.00 59.51	
	ATOM	24	CD	ARG		3	66.375	29.629	10.048	1.00 61.41	
35	MOTA	25	NE	ARG		3	66.440	28.471	10.927	1.00 61.03	
00	ATOM	26	CZ	ARG		3	67.550	27.787	11.159	1.00 62.03	
	ATOM	27		ARG		3	68.692	28.169	10.586	1.00 60.01	
	ATOM	28		ARG		3	67.509	26.694	11.918	1.00 62.76	
	ATOM	29	C	ARG		3	64.034	30.659	6.055	1.00 59.92	
40	ATOM .	30	0	ARG		3	62.883	30.487	6.454	1.00 59.64	
40	ATOM	31	N	ALA		4	64.395	31.685	5.291	1.00 57.25	
		32	CA	ALA		4	63.404	32.641	4.836	1.00 55.16	
	MOTA MOTA	33	CB	ALA		4	64.065	33.782	4.088	1.00 53.78	
	ATOM	34	CP	ALA		4	62.421	31.917	3.927	1.00 54.69	
45		35		ALA		4	61.213	32.062	4.074	1.00 55.60	
40	ATOM	36	N O	ASP		5	62.942	31.127	2.995	1.00 54.79	
	MOTA			ASP		5	62.097	30.392	2.060	1.00 55.84	
	MOTA	37 38	CA CB	ASP		5	62.937	29.580	1.058	1.00 56.83	
	ATOM			ASP		5	63.918	30.437	0.278	1.00 59.97	
50	MOTA	39				5	63.519	31.519	-0.213	1.00 61.60	
50	ATOM	40		ASP		5	65.095	30.025	0.148	1.00 62.19	
	ATOM	41		ASP			61.176	29.443	2.815	1.00 55.90	
	ATOM	42	C	ASP		5 5	60.011	29.268	2.445	1.00 53.57	
	MOTA	43	0	ASP		6	61.695	28.832	3.877	1.00 55.26	
55	ATOM	44	N	ILE				27.889	4.650	1.00 55.12	
55	MOTA	45	CA	ILE		6	60.890 61.743	27.883	5.657	1.00 55.82	
	MOTA	46		ILE		6	60.878	26.056	6.354	1.00 53.18	
	MOTA	47		ILE		6 6	62.924	26.056	4.933	1.00 56.24	
	MOTA	48		ILE		6 6	63.802	25.568	5.816	1.00 50.2	
60	ATOM	49				6	59.742	28.561	5.396	1.00 54.7	
υo	MOTA	50	С	ILE	A	J	33.144	20.301	5.550	1.00 Ja.1.	

	WO 01/5895	51					PCT/EP01/01457			
						-73				
	ATOM	51	0	ILE A	6	58.589	28.159	5.256	1.00 55.75	8
•	ATOM	52	N	LEU A	7	60.058	29.583	6.182	1.00 52.58	7
	ATOM	53	CA	LEU A	7	59.041	30.299	6.929	1.00 51.88	6
_	ATOM	54	CB	LEU A	7	59.697	31.387	7.784	1.00 51.65	6
5	MOTA	55	CG	LEU A	7	60.589	30.828	8.895	1.00 51.59	6
	MOTA	56		LEU A	7	61.484	31.902	9.480	1.00 51.45	6
	MOTA	57		LEU A	7	59.700	30.225	9.953	1.00 51.32	6
	MOTA	58		LEU A	7	58.048	30.915 30.921	5.961 6.204	1.00 51.46 1.00 51.87	6 8
10·	MOTA	59 60	0	LEU A TYR A	7 8	56.846 58.561	30.921	4.848	1.00 51.87	7
10	ATOM ATOM	60 61	N CA	TYR A	8	57.727	32.041	3.832	1.00 53.61	6
	ATOM	62	CB	TYR A	8	58.601	32.520	2.672	1.00 55.43	6
	ATOM	63	CG	TYR A	8	57.806	33.119	1.543	1.00 57.65	6
	ATOM	64	CD1		8	57.217	34.379	1.668	1.00 58.24	6
15	ATOM	65	CE1	TYR A	8	56.439	34.914	0.644	1.00 58.94	6
	MOTA	66	CD2	TYR A	8	57.601	32.407	0.366	1.00 58.93	6
	ATOM	67	CE2	TYR A	8	56.825	32.930	-0.665	1.00 60.13	6
	MOTA	68	CZ	TYR A	8	56.244	34.183	-0.518	1.00 60.03	6
00	ATOM	69	OH	TYR A	8	55.453	34.699	-1.527	1.00 63.97	8 6
20	MOTA	70	C	TYR A	8	56.636	31.114	3.296	1.00 52.67 1.00 52.13	8
	MOTA	71	N O	TYR A ASN A	8 9	55.483 57.009	31.511 29.880	3.143 2.997	1.00 53.39	7
	MOTA MOTA	72 73	·CA	ASN A	9	56.051	28.918	2.488	1.00 53.87	6
	ATOM	74	CB	ASN A	9	56.750	27.613	2.096	1.00 58.21	6
25	ATOM	75	CG	ASN A	9	57.646	27.772	0.860	1.00 62.45	6
	ATOM	76		ASN A	9	57.647	28.824	0.209	1.00 64.72	8
	MOTA	77	ND2	ASN A	9	58.405	26.724	0.530	1.00 62.99	7
	MOTA	78	C.	ASN A	9	54.987	28.638	3.526	1.00 53.31	6
	MOTA	79	0	ASN A	9	53.794	28.725	3.239	1.00 52.02	8
30	MOTA	80	N	ILE A	10	55.420	28.300	4.736	1.00 53.77	7
	MOTA	81	CA	ILE A	10	54.489	28.018	5.829	1.00 55.18	6
	ATOM	82	CB	ILE A	10	55.229	27.788	7.150	1.00 53.51	6 6
	MOTA	83		ILE A	10	54.220 56.109	27.639 26.541	8.272 7.044	1.00 53.99 1.00 50.48	6
35	MOTA MOTA	84 85		ILE A	10 10	57.043	26.346	8.202	1.00 30.48	6
00	ATOM	86	CDI	ILE A	10	53.523	29.183	6.032	1.00 57.42	6
	ATOM	87	o	ILE A	10	52.319	28.997	6.221	1.00 57.74	8
	ATOM	88	N	ARG A	11	54.070	30.390	5.997	1.00 58.29	7
	ATOM	89	CA	ARG A	11	53.283	31.600	6.156	1.00 60.48	6
40	ATOM	90	CB	ARG A	11	54.199	32.810	6.042	1.00 64.72	6
	MOTA	91	CG	ARG A	11	53.513	34.134	6.270	1.00 70.99	6
	MOTA	92	CD	ARG A	11	53.241	34.337	7.757	1.00 79.75	6
	ATOM	93	NE	ARG A	11	53.059	35.751	8.105	1.00 86.33	7
15	MOTA	94	CZ	ARG A	11	53.848	36.733 36.451	7.665 6.845	1.00 89.85 1.00 92.68	6 7
45	ATOM	95 96		ARG A	11 11	54.871 53.636	37.992	8.056	1.00 90.02	7
	ATOM ATOM	97	C	ARG A	11	52.204	31.701	5.082	1.00 59.54	6
	MOTA	98.		ARG A	11	51.038	31.954	5.363	1.00 59.64	8
	ATOM	99	N	GLN A	12	52.614	31.489	3.841	1.00 59.22	7
50	ATOM	100	CA		12	51.718	31.595	2.705	1.00 58.15	6
	MOTA	101	СВ	GLN A	12	52.542	31.776	1.441	1.00 59.05	6
	MOTA	102	CG	GLN A	12	52.118	32.961	0.629	1.00 60.64	6
	MOTA	103	CD	GLN A	12	52.674	34.226	1.192	1.00 61.53	6
	MOTA	104		GLN A	12	53.879	34.345	1.360	1.00 65.50	8
55	ATOM	105		GLN A	12	51.811		1.489	1.00 62.18	7
	ATOM	106	C	GLN A		50.732	30.460 30.651	2.472 1.814	1.00 57.30 1.00 57.03	6 8
	ATOM	107	N O	GLN A THR A		49.714 51.029	29.280	2.987	1.00 57.03	8 7
	ATOM ATOM	108 109	CA	THR A		50.142	28.147	2.773	1.00 57.26	6
60	ATOM	110	CB	THR A		50.922	26.964	2.186	1.00 57.20	6
	ATOM	111		THR A		52.000	26.616	3.071	1.00 55.40	8

							-74				
	ATOM	112	CG2	THR A	Ą	13	51.477	27.326	0.813	1.00 58.15	6
	ATOM	113		THR A		13	49.411	27.650	4.013	1.00 58.45	6
	ATOM	114		THR A		13	48.423	26.932	3.905	1.00 58.36	8
	ATOM	115	N	SER A	Α	14	49.892	28.034	5.187	1.00 60.01	7
5	ATOM	116	CA	SER A	A	14	49.290	27.584	6.424	1.00 60.03	6
	MOTA	117	CB	SER A	A	14	50.198	27.930	7:601	1.00 61.46	6
	MOTA	118	OG	SER A	A	14	49.813	27.207	8.758	1.00 65.18	8
	MOTA	119	С	SER I	A	14	47.899	28.147	6.664	1.00 59.50	6
	ATOM	120	0	SER I	A	14	47.560	29.240	6.189	1.00 58.72	8
10	MOTA	121	N	ARG A		15	47.102	27.377	7.407	1.00 58.04 1.00 55.62	7 6
	MOTA	122	CA	ARG .		15	45.740	27.753	7.755	1.00 55.62	6
	MOTA	123	СВ	ARG A		15	44.744	26.996 27.253	6.877 5.385	1.00 50.74	6
	MOTA	124	CG	ARG		15	44.925 43.688	26.851	4.614	1.00 53.02	6
15	MOTA	125	CD	ARG A		15 15	42.519	27.540	5.151	1.00 64.02	7
15	ATOM	126	NE CZ	ARG .		15	41.261	27.216	4.870	1.00 65.48	6
	MOTA	127 128		ARG		15	41.007	26.201	4.050	1.00 67.33	7
	ATOM ATOM	129		ARG		15	40.256	27.908	5.408	1.00 64.23	7
	ATOM	130	C	ARG		15	45.516	27.420	9.219	1.00 52.12	6
20	ATOM	131	Ö	ARG		15	45.135	26.310	9.562	1.00 53.25	8
	ATOM	132	N	PRO		16	45.751	28.392	10.104	1.00 50.04	7
	ATOM	133	CD	PRO		16	46.198	29.750	9.773	1.00 48.52	6
	ATOM	134	CA	PRO		16	45.597	28,249	11.551	1.00 49.56	6
	ATOM	135	CB	PRO	Α	16	45.959	29.634	12.073	1.00 49.66	6
25	ATOM	136	CG	PRO	Α	16	46.870	30.165	11.041	1.00 49.57	6
	MOTA	137	C	PRO	Α	16	44.215	27.816	12.016	1.00 50.11	6
	ATOM	138	0	PRO	Α	16	44.060	27.322	13.131	1.00 51.27	8
	ATOM	139	N	ASP		17	43.208	28.013	11.176	1.00 50.70	7
	MOTA	140	CA	ASP		17	41.856	27.640	11.548	1.00 50.64	6 6
30	MOTA	141	CB	ASP		17	40.850	28.609	10.931	1.00 54.16	6
	ATOM	142	CG	ASP		17	40.873	29.974	11.592	1.00 59.76 1.00 60.67	8
	ATOM	143		ASP		17	41.245	30.060	12.791 10.920	1.00 62.99	8
	ATOM	144		ASP		17	40.500 41.482	30.965 26.218	11.157	1.00 50.71	6
35	MOTA	145	C	ASP ASP		17 17	40.353	25.783	11.390	1.00 48.36	8
33	MOTA	146 147	O N	VAL		18	42.429	25.484	10.583	1.00 51.85	7
	ATOM ATOM	148	CA	VAL		18	42.143	24.128	10.148	1.00 52.53	б
	ATOM	149	CB	VAL		18	42.262	24.011	8.622	1.00 53.05	6
	ATOM	150		VAL		18	41.834	22.618	8.169	1.00 51.38	6
40	ATOM	151		VAL		18	41.396	25.077	7.963	1.00 51.76	6
• •	ATOM	152	С	VAL	Α	18	42.993	23.050	10.779	1.00 52.56	6
	ATOM	153	0	VAL	Α	18	44.199	23.006	10.588	1.00 52.64	8
	ATOM	154	N	ILE	Α	19	42.327	22.172	11.519	1.00 53.41	7
	ATOM	155	CA	ILE		19	42.954	21.042	12.202	1.00 52.70	6
45	MOTA	156	CB	ILE		19	41.871	20.319	13.072	1.00 52.71	6
	MOTA	157		ILE		19	40.819	19.671	12.190	1.00 52.40	6
	MOTA	158		ILE		19	42.504	19.290	13.992	1.00 53.50 1.00 50.39	6 6
	MOTA	159		ILE		19	41.546	18.811	15.056	1.00 50.39	6
50	MOTA	160	C	ILE		19	43.596	20.097 19.687	11.164 10.193	1.00 52.30	8
50	MOTA	161	0	ILE		19	42.957	19.007	11.355	1.00 51.35	7
	ATOM	162	N	PRO		20 20	44.878 45.711	20.210	12.472	1.00 54.14	6
	ATOM	163	CD	PRO PRO		20	45.644	18.876	10.461	1.00 56.34	6
	MOTA	164 165	CA CB	PRO		20	47.078	18.996	10.981	1.00 56.60	6
55	ATOM ATOM	166	CG	PRO		20	47.060	20.235	11.840	1.00 58.05	6
55	MOTA	167	C	PRO		20	45.177	17.432	10.474	1.00 58.61	6
	MOTA	168	Ö	PRO		20	45.974	16.523	10.682	1.00 59.22	8
	ATOM	169	N	THR		21	43.886	17.231	10.246	1.00 62.30	7
	ATOM	170		THR		21	43.283	15.900	10.236	1.00 66.91	6
60	ATOM	171	СВ	THR	Α	21	41.765	16.020	10.495	1.00 65.83	6
	MOTA	172	OG1	THR	Α	21	41.516	15.813	11.883	1.00 67.19	8

PCT/EP01/01457

WO 01/58951 -75 ATOM MOTA MOTA 9.179 1.00 74.54 .7 MOTA 6 MOTA 6 MOTA 6 MOTA MOTA MOTA 7 10 атом 6 MOTA 8 MOTA 7 ATOM MOTA 15 ATOM 6 б MOTA 6 MOTA 7 MOTA MOTA 20 7 ATOM 7 MOTA 6 MOTA MOTA 7 ATOM 25 ATOM 6 MOTA 6 MOTA 8 MOTA 8 MOTA 202 C ASP A 24 39.631 10.021 11.305 1.00 84.31 203 O ASP A 24 39.173 9.975 12.458 1.00 84.64 204 N ARG A 25 40.935 9.981 11.029 1.00 81.75 205 CA ARG A 25 41.936 9.898 12.091 1.00 79.08 206 CB ARG A 25 43.309 9.539 11.527 1.00 81.87 207 CG ARG A 25 43.471 8.100 11.087 1.00 86.55 208 CD ARG A 25 44.960 7.785 10.851 1.00 90.81 209 NE ARG A 25 45.187 6.380 10.489 1.00 95.61 210 CZ ARG A 25 46.388 5.815 10.345 1.00 96.85 211 NH1 ARG A 25 47.495 6.537 10.530 1.00 97.46 212 NH2 ARG A 25 46.487 4.522 10.023 1.00 97.32 213 C ARG A 25 42.059 11.201 12.870 1.00 75.12 214 O ARG A 25 42.059 11.201 12.870 1.00 75.55 215 N PRO A 26 42.034 11.112 14.212 1.00 70.63 216 CD PRO A 26 41.636 9.933 14.999 1.00 69.09 217 CA PRO A 26 42.152 12.281 15.083 1.00 67.24 218 CB PRO A 26 41.802 11.723 16.460 1.00 67.68 219 CG PRO A 26 40.930 10.565 16.158 1.00 68.06 30 MOTA ATOM 8 7 ATOM 6 MOTA 6 ATOM 35 атом 6 MOTA 7 MOTA MOTA MOTA 40 MOTA MOTA MOTA MOTA MOTA 45 MOTA ATOM 40.930 10.565 16.158 1.00 68.06 CG PRO A 26 ATOM 219 43.593 12.762 15.053 1.00 64.53 44.491 12.000 14.694 1.00 63.60 43.816 14.020 15.420 1.00 61.16 PRO A 26 6 MOTA 220 C O PRO A 26 N VAL A 27 CA VAL A 27 221 O 222 N 8 MOTA 7 50 MOTA 45.168 14.544 15.476 1.00 57.20 MOTA 223 224 CB VAL A 27 45.197 16.079 15.374 1.00 56.96 MOTA 46.535 16.615 15.872 1.00 54.60 44.986 16.496 13.930 1.00 55.09 CG1 VAL A 27 6 225 MOTA 226 CG2 VAL A 27 227 C VAL A 27 228 O VAL A 27 229 N ALA A 28 44.986 45.685 6 MOTA 14.114 16.835 1.00 55.33 55 6 ATOM 45.026 14.328 17.849 1.00 53.70 45.026 14.320 17.033 46.852 13.484 16.858 1.00 54.55 47.405 13.023 18.118 1.00 53.25 48.250 11.785 17.907 1.00 52.00 48.230 14.117 18.761 1.00 52.77 49.324 14.451 18.294 1.00 52.53 MOTA MOTA 6 230 CA ALA A 28 MOTA 231 CB ALA A 28 232 C ALA A 28 233 O ALA A 28 MOTA 6 60 MOTA

MOTA

							-76					
	ATOM	234	N	VAL A	29		47.683	14.672	19.837	1.00	51.33	7
	ATOM	235	CA	VAL A	29		48.332	15.730	20.590		49.28	6
	ATOM	236	СВ	VAL A	29		47.367	16.921	20.845		47.59	6
	ATOM	237		VAL A	29		48.056	17.985	21.676		44.30	6
5	MOTA	238		VAL A	29		46.891	17.497	19.527	1.00	44.21	6
_	MOTA	239	C	VAL A	29		48.782	15.171	21.930	1.00	49.54	· 6
	MOTA	240	Ō	VAL A	29		48.014	14.524	22.635		49.14	8
	ATOM	241	N	SER A	30		50.043	15.402	22.261		49.54	7
	ATOM	242	CA	SER A	30		50.574	14.946	23.523	1.00	52.38	6
10	ATOM	243	CB	SER A	30		51.869	14.163	23.309	1.00	51.50	6
	MOTA	244	OG	SER A	30		52.846	14.945	22.645	1.00	56.10	8
	MOTA	245	С	SER A	30		50.819	16.187	24.362	1.00	54.25	6
	MOTA	246	0	SER A	30		51.360	17.174	23.880	1.00	56.41	8
	MOTA	247	N	VAL A	31		50.396	16.134	25.618		56.86	7
15	MOTA	248	CA	VAL A	31		50.543	17.258	26.531		58.42	6
	ATOM	249	CB	VAL A	31		49.170	17.768	27.012		58.48	6
	MOTA	250		VAL A	31		49.338	19.086	27.744		59.95	6
	MOTA	251		VAL A	31		48.219	17.910	25.835		56.73	6
00	ATOM	252	C	VAL A	31		51.328	16.803	27.747		59.56	6
20	MOTA	253	0	VAL A	31		51.073	15.729	28.281		60.85	8
	MOTA	254	N	SER A	32		52.271	17.631	28.185		61.06	7 6
	MOTA	255	CA	SER A	32 32		53.105 54.388	17.312 16.619	29.338 28.868		60.16 59.88	6
•	ATOM ATOM	256 257	CB OG	SER A SER A	32		55.294	16.430	29.937		60.41	8
25	ATOM	258	C	SER A	32		53.465	18.568	30.116		60.19	6
20	ATOM	259	o	SER A	32		54.206	19.416	29.621		61.87	8
	MOTA	260	N	LEU A	33		52.946	18.689	31.333		58.89	7
	ATOM	261	CA	LEU A	33		53.256	19.847	32.170		57.23	6
	ATOM	262	CB	LEU A	33	•	52.112	20.142	33.142		55.20	6
30	ATOM	263	CG	LEU A	33		50.740	20.363	32.511	1.00	54.66	6
	ATOM	264	CD1	LEU A	33		49.762	20.880	33.543	1.00	51.01	6
	ATOM	265	CD2	LEU A	33		50.880	21.342	31.373		55.39	6
	MOTA	266	С	LEU A	33		54.518	19.601	32.979		56.76	6
	ATOM	267	0	LEU A	33		54.697	18.526	33.533		58.14	8
35	MOTA	268	N	LYS A	34		55.394	20.597	33.028		57.17	7
	ATOM	269	CA	LYS A	34		56.633	20.512	33.800		57.46	6
	ATOM	270	CB	LYS A	34		57.865	20.690	32.910		60.89	6
	MOTA	271	CG	LYS A	34		57.940	19.723	31.738		68.80	6
40	ATOM	272	CD	LYS A	34		58.048	18.249	32.186		73.30	6
40	MOTA	273	CE	LYS A	34		58.071 58.210	17.290 15.842	30.961 31.340		74.90 75.55	6 7
	ATOM	274 275	NZ C	LYS A	34 34		56.522	21.691	34.741		54.81	6
	ATOM ATOM	275	0	LYS A	34		56.567	22.834	34.308		55.33	8
	ATOM	277	N	PHE A	35		56.358	21.422	36.026		52.88	7
45	ATOM	278	CA	PHE A	35		56.215	22.507	36.976		50.00	6
	ATOM	279	СВ	PHE A	35		55.586	21.993	38.260		45.71	6
	ATOM	280	CG	PHE A	35		54.186	21.542	38.072		45.07	6
	ATOM	281		PHE A	35		53.912	20.256	37.634		45.46	. 6
	ATOM	282	CD2	PHE A	35		53.133	22.429	38.252	1.00	47.46	6
50	MOTA	283	CE1	PHE A	35		52.612	19.848	37.372	1.00	45.03	6
	MOTA	284	CE2	PHE A	35		51.819	22.036	37.990		49.48	6
	MOTA	285	$^{\rm cz}$	PHE A	35		51.560	20.735	37.547		48.14	6
	MOTA	286	C	PHE A	35		57.494	23.268	37.247		49.05	6
EE	ATOM	287	0	PHE A	35		58.549	22.687	37.480		48.49	8
55	MOTA	288	N	ILE A	36		57.374	24.588	37.191 37.393		46.86 45.55	7
	ATOM	289	CA	ILE A	36 36		58.492 58.538	25.482 26.551	36.284		43.55	6 6
	MOTA MOTA	290 291	CB CG2	ILE A	36		59.771	27.411	36.433		39.03	6
	ATOM	291		ILE A	36		58.526	25.876	34.917		44.17	6
60	MOTA	293		ILE A	36		59.671	24.916	34.699		46.33	6
	ATOM	294	C	ILE A	36		58.392	26.181	38.739		46.38	6
							•					

	WO 01/589	51							PCT/EP01/014	1 57
						-77				
	ATOM ATOM	295 296	O N	ILE A ASN A	36 37	59.405 57.176	26.580 26.340	39.318 39.244	1.00 45.40 1.00 46.13	8 7
	ATOM	297	CA	ASN A	37	57.023	27.008	40.526	1.00 46.13	6
_	MOTA	298	СВ	ASN A	37	57.491	28.462	40.400	1.00 46.32	6
5	ATOM	299	CG	ASN A	37	58.009	29.030	41.707	1.00 48.59	6
	MOTA MOTA	300 301		ASN A ASN A	37 37	57.408 59.124	28.844 29.743	42.759	1.00 49.38 1.00 46.71	8
	ATOM	302	C	ASN A	37	55.595	26.975	41.639 41.046	1.00 46.71	7 6
	MOTA	303	Ö	ASN A	37	54.644	26.799	40.281	1.00 44.02	8
10	MOTA	304	N	ILE A	38	55.465	27.117	42.362	1.00 46.64	7
	MOTA	305	CA	ILE A	38	54.173	27.158	43.033	1.00 48.46	6
	ATOM	306	CB CG2	ILE A	38	53.988	25.951	43.923	1.00 47.34	6
	ATOM ATOM	307 308		ILE A	38 38	52.680 53.983	26.066 24.697	44.671 43.050	1.00 49.13 1.00 48.40	6 6
15	ATOM	309		ILE A	38	54.079	23.402	43.791	1.00 47.55	6
	MOTA	310	С	ILE A	38	54.245	28.433	43.847	1.00 50.74	6
	MOTA	311	0	ILE A	38	54.979	28.505	44.817	1.00 53.13	8
	ATOM	312 313	N	LEU A	39	53.485	29.438	43.433	1.00 53.46	7
20	MOTA MOTA	314	CA CB	LEU A	39 39	53.527 53.350	30.757 31.806	44.045 42.952	1.00 55.16 1.00 54.91	6 6
	ATOM	315	CG	LEU A	39	54.330	31.591	41.800	1.00 57.26	6
	ATOM	316		LEU A	39	54.108	32.647	40.728	1.00 54.71	6
	MOTA	317		LEU A	39	55.757	31.623	42.341	1.00 54.68	6
25	ATOM	318	С	LEU A	39	52.613	31.098	45.203	1.00 56.69	6
20	ATOM ATOM	319 320	O N	LEU A GLU A	39 40	53.043 51.352	31.750 30.715	46.157 45.123	1.00 59.24 1.00 56.60	8 7
	ATOM	321	CA	GLU A	40	50.451	31.019	46.216	1.00 58.75	6
	ATOM	322	CB	GLU A	40	49.617	32.251	45.920	1.00 59.61	6
20	MOTA	323	CG	GLU A	40	50.426	33.520	45.821	1.00 65.69	6
30	ATOM ATOM	324 325	CD OE1	GLU A GLU A	40 40	49.547 48.747	34.752 34.812	45.683 44.715	1.00 69.26 1.00 72.53	6
	ATOM	326	OE2		40	49.655	35.659	46.543	1.00 72.33	8 8
	MOTA	327	C	GLU A	40	49.534	29.863	46.448	1.00 60.49	6
0.5	MOTA	328	0	GLU A	40	49.006	29.275	45.509	1.00 62.83	8
35	ATOM	329	N	VAL A	41	49.348	29.525	47.710	1.00 60.13	7
	ATOM ATOM	330 331	CA CB	VAL A	41 41	48.474 49.292	28.431 27.230	48.049 48.576	1.00 60.14 1.00 59.98	6 6
	MOTA	332		VAL A	41	48.376	26.185	49.146	1.00 59.73	6
	MOTA	333	CG2	VAL A	41	50.118	26.632	47.444	1.00 59.26	6
40	MOTA	334	С	VAL A	41	47.510	28.934	49.109	1.00 60.58	6
	ATOM ATOM	335 336	O N	VAL A ASN A	41 42	47.864 46.283	29.793 28.428	49.934 49.059	1.00 61.24 1.00 59.54	8 7
	ATOM	337	CA	ASN A	42	45.267	28.806	50.024	1.00 60.72	6
	ATOM	338	CB	ASN A	42	44.346	29.895	49.463	1.00 59.36	6
45	MOTA	339	CG	ASN A	42	43.473	30.530	50.533	1.00 59.07	6
	ATOM	340		ASN A	42	42.811	29.835	51.303	1.00 60.43	8
	ATOM ATOM	341 342	C MD2	ASN A ASN A	42 42	43.462 44.474	31.856 27.535	50.582 50.286	1.00 57.17 1.00 62.57	7 6
	MOTA	343	ō	ASN A	42	43.654	27.107	49.460	1.00 62.42	8
50	MOTA	344	N	GLU A	43	44.731	26.921	51.435	1.00 63.02	7
	MOTA	345	CA	GLU A	43	44.045	25.695	51.792	1.00 62.62	6
	ATOM ATOM	346 347	CB CG	GLU A	43 43	44.772 44.206	25.004	52.942	1.00 65.20 1.00 67.62	6
	ATOM	348	CD	GLU A	43	45.088	23.642 22.827	53.253 54.174	1.00 67.62	6 6
55	MOTA	349		GLU A	43	44.628	21.739	54.581	1.00 71.48	8
	MOTA	350		GLU A	43	46.228	23.256	54.479	1.00 67.83	8
	ATOM	351	C	GLU A	43	42.595	25.959	52.169	1.00 61.53	6
	ATOM ATOM	352 353	N O	GLU A ILE A	43 44	41.755 42.309	25.058	52.086	1.00 59.68	8
60	MOTA	354	CA	ILE A	44	40.957	27.197 27.580	52.575 52.951	1.00 60.06 1.00 60.59	7 6
	MOTA	355	СВ	ILE A	44	40.923	28.953	53.632	1.00 60.98	6

							-78					
	ATOM	356	CG2	ILE	A	44	39.469	29.343	53.943	1.00	61.06	6
	ATOM	357		ILE		44	41.749	28.921	54.918	1.00	61.51	6
	MOTA	358	CD1	ILE		44	41.119	28,117	56.022	1.00	61.37	6
	MOTA	359	С	ILE	A	44	40.069	27.660	51.718	1.00	61.06	6
5	MOTA	360	0	ILE	A	44	38.942	27.148	51.708	1.00	61.53	8
	MOTA	361	N	THR	Α	45	40.581	28.302	50.674	1.00	60.25	7
	MOTA	362	CA	THR	Α	45	39.826	28.464	49.426	1.00		6
	MOTA	363	CB	THR	A	45	40.086	29.844	48.805	1.00		6
	MOTA	364	OG1	THR		45	41.492	29.992	48.535	1.00		8
10	ATOM	365	CG2	THR		45	39.632	30.934	49.762	1.00		6
	ATOM	366	С	THR		45	40.139	27.407	48.374	1.00	-	6
	MOTA	367	0	THR		45	39.465	27.328	47.349		54.64	8
	MOTA	368	N	ASN		46	41.169	26.607	48.620	1.00		7
46	MOTA	369	CA	ASN		46	41.534	25.563	47.677	1.00		6 6
15	ATOM	370	CB	ASN		46	40.390	24.557	47.560	1.00	56.92	6
	ATOM	371	CG OD1	ASN		46	40.612 39.671	23.327 22.621	48.412 48.746		55.85	8
	ATOM	372		ASN ASN		46 46	41.866	23.058	48.754	1.00		7
	ATOM	373 374	C	ASN		46	41.869	26.127	46.299	1.00		6
20	ATOM ATOM	375	0	ASN		46	41.350	25.659	45.283		58.80	8
20	ATOM	376	Ŋ	GLU		47	42.744	27.130	46.275		54.91	7
	ATOM	377	CA	GLU		47	43.156	27.766	45.044		52.39	6
	ATOM	378	CB	GLU		47	42.606	29.183	44.999		50.63	6
	ATOM	379	CG	GLU		47	41.107	29.247	44.938		48.77	6
25	ATOM	380	CD	GLU		47	40.601	30.675	44.951	1.00	53.28	6
	ATOM	381		GLU	Α	47	41.370	31.577	44.568	1.00	51.68	8
	MOTA	382	OE2	GLU	Α	47	39.429	30.902	45.333	1.00	58.43	8
	MOTA	383	С	GLU	Α	47	44.671	27.776	44.979	1.00	52.87	6
	MOTA	384	0	GLU	Α	47	45.347	28.009	45.981	1.00	53.20	8
30	MOTA	385	N	VAL	Α	48	45.208	27.513	43.797	1.00	53.53	7
	MOTA	386	CA	VAL	Α	48	46.656	27.481	43.619		53.36	6
	MOTA	387	CB	VAL		48	47.147	26.043	43.318		53.31	6
	MOTA	388		VAL		48	48.646	26.029	43.122		55.73	6
0=	ATOM	389		VAL		48	46.781	25.130	44.456		52.72	6
35	ATOM	390	С	VAL		48	47.108	28.390	42.484		52.90	6
	MOTA	391	0	VAL		48	46.441	28.504	41.454		54.54	8
	MOTA	392	N	ASP		49	48.242	29.046	42.691		52.21	7
	ATOM	393	CA	ASP		49	48.818	29.928	41.692		51.57	6
40	ATOM	394	CB	ASP		49	49.084 49.264	31.291	42.304		52.64 53.86	6 6
40	MOTA	395	CG OD1	ASP ASP		49 49	49.264	32.352 32.051	41.268 40.246		54.56	8
	ATOM ATOM	396 397 -		ASP		49	48.779	33.482	41.474		57.00	8
	ATOM	398	C	ASP		49	50.121	29.241	41.313		50.45	6
	ATOM	399	0	ASP		49	51.074	29.254	42.075	_	52.15	8
45	MOTA	400	N	VAL		50	50.155	28.636	40.135		49.83	7
. •	ATOM	401	CA	VAL		50	51.329	27.893	39.711		49.77	6
	ATOM	402	CB	VAL		50	50.992	26.372	39.723		51.61	6
	MOTA	403		VAL		50	50.095	26.015	38.531		51.90	6
	MOTA	404		VAL		50	52.265	25.539	39.721		53.03	6
50	ATOM	405	С	VAL		50	51.890	28.290	38.335		49.01	6
	ATOM	406	0	VAL	Α	50	51.193	28.878	37.508	1.00	50.33	8
	ATOM	407	N	VAL	Α	51	53.163	27.974	38.117	1.00	46.39	7
	ATOM	408	CA	VAL	Α	51	53.863	28.245	36.861	1.00	45.41	6
	MOTA	409	CB	VAL		51	55.111	29.134	37.083		43.93	6
55	MOTA	410	CG1	VAL	Α	51	55.943	29.182	35.807		42.09	6
	MOTA	411		VAL		51	54.696	30.536	37.497		41.05	6
	ATOM	412	С	VAL		51	54.336	26.899	36.291		46.83	6
	ATOM	413	0	VAL		51	54.879	26.063	37.016		47.95	8
60	ATOM	414	N	PHE		52	54.147	26.684	34.996		45.38	7
60	MOTA	415	CA	PHE		52	54.560	25.423	34.402		44.58	6
	MOTA	416	СВ	PHE	A	52	53.485	24.373	34.662	1.00	44.09	6

							-79				
	MOTA	417	CG	PHE A	A !	52	52.155	24.718	34.068	1.00 43.27	6
	ATOM	418	CD1	PHE A	Α !	52	51.857	24.393	32.758	1.00 42.79	6
	ATOM	419	CD2	PHE A	A !	52	51.211	25.411	34.805	1.00 45.35	6
	ATOM	420	CE1	PHE A	A !	52	50.643	24.755	32.194	1.00 41.86	6
5	MOTA	421	CE2	PHE 2	A !	52	49.991	25.776	34.240	1.00 45.03	6
	MOTA	422	CZ	PHE 2		52	49.712	25.445	32.933	1.00 41.04	6
	MOTA	423	С	PHE A	A !	52	54.789	25.547	32.906	1.00 45.52	6
	MOTA	424	0	PHE 3		52	54.403	26.536	32.288	1.00 46.49	8
	ATOM	425	N	TRP 2		53	55.431	24.541	32.328	1.00 45.07	7
10	ATOM	426	CA	TRP .	Α	53	55.662	24.527	30.898	1.00 46.61	6
	ATOM	427	CB	TRP 3		53	57.043	24.000	30.573	1.00 48.36	6
	MOTA	428	CG	TRP .		53	58.137	24.899	30.983	1.00 50.29	6
	MOTA	429		TRP .		53	59.531	24.604	30.942	1.00 50.34	6
	MOTA	430	CE2	TRP .		53	60.213	25.755	31.386	1.00 51.89	6
15	ATOM	431		TRP .		53	60.274	23.473	30.570	1.00 52.05	6
	MOTA	432		TRP .		53	58.024	26.175	31.436	1.00 50.84	6
	MOTA	433		TRP .		53	59.267	26.700	31.682	1.00 52.12	7
	MOTA	434		TRP		53	61.605	25.817	31.470	1.00 53.79	6
	MOTA	435	CZ3	TRP		53	61.660	23.527	30.649	1.00 53.82	6 6
20	MOTA	436		TRP		53	62.314	24.697	31.099	1.00 55.14	6
	MOTA	437	С	TRP		53	54.644	23.599	30.285	1.00 47.55	8
	MOTA	438	0	TRP		53	54.645	22.410	30.564		7
	MOTA	439	N	GLN		54	53.765	24.139	29.457	1.00 47.91 1.00 48.38	6
0=	MOTA	440	CA	GLN		54	52.765	23.312	28.825	1.00 48.38	6
25	MOTA	441	CB	GLN		54	51.517	24.132	28.529	1.00 47.36	6
	ATOM	442	CG	GLN		54	50.322	23.309	28.095	1.00 54.00	6
	ATOM	443	CD	GLN		54	49.001	24.016 24.360	28.375 29.515	1.00 53.48	8
	ATOM	444		GLN		54	48.697	24.231	27.335	1.00 57.12	7
20	ATOM	445	NE2	GLN		54 54	48.209 53.378	22.755	27.555	1.00 37.12	6
30	ATOM	446	C	GLN		54	53.095	23.203	26.453	1.00 50.86	8
	ATOM	447	0	GLN GLN		55	54.251	21.779	27.738	1.00 50.50	7
	MOTA	448	N CA	GLN		55	54.937	21.122	26.641	1.00 52.90	6
	MOTA	449 450	CB	GLN		55	55.995	20.200	27.234	1.00 58.12	6
35	ATOM ATOM	451	CG	GLN		55	56.699	19.288	26.263	1.00 66.05	6
00	ATOM	452	CD	GLN		55	57.909	18.634	26.907	1.00 71.07	6
	MOTA	453		GLN		55	57.890	18.307	28.107	1.00 73.93	8
	ATOM	454		GLN		55	58.969	18.442	26.123	1.00 72.99	7
	ATOM	455	C	GLN		55	53.939	20.353	25.774	1.00 51.30	6
40	ATOM	456	ō	GLN		55	53.451	19.293	26.151	1.00 50.67	8
	ATOM	457	N	THR		56	53.648	20.907	24.604	1.00 49.14	7
	ATOM	458	CA	THR		56	52.690	20.325	23.684	1.00 46.69	6
	ATOM	459	СВ	THR		56	51.597	21.347	23.342	1.00 45.67	6
	ATOM	460	OG1	THR	Α	56	51.138	21.969	24.541	1.00 45.84	8
45	MOTA	461	CG2	THR	Α	56	50.426	20.673	22.666	1.00 45.93	6
	ATOM	462	С	THR	Α	56	53.344	19.878	22.389	1.00 46.05	б
	ATOM	463	0	THR	Α	56	54.286	20.503	21.917	1.00 46.13	8
	ATOM	464	N	THR	A	57	52.836	18.796	21.812	1.00 44.22	7
	ATOM	465	CA	THR	Α	57	53.384	18.286	20.569	1.00 44.65	6
50	ATOM	466	CB	$\mathbf{T}\mathbf{H}\mathbf{R}$	Α	57	54.511	17.270	20.823	1.00 44.59	6
	ATOM	467	OG1	THR	Α	57	55.593	17.914	21.499	1.00 42.38	8
	MOTA	468	CG2	THR	Α	57	55.036	16.733	19.512	1.00 49.11	6
	MOTA	469	С	THR		57	52.316	17.627	19.721	1.00 43.97	6
	MOTA	470	0	THR	Α	57	51.377	17.039	20.239	1.00 44.62	8
55	MOTA	471	N	TRP		58	52.452	17.753	18.410	1.00 42.72	7
	MOTA	472	CA	TRP		58	51.502	17.153	17.489	1.00 44.75	6
	MOTA	473	CB	TRP		58	50.139	17.883	17.529	1.00 42.24	. 6
	MOTA	474	CG	TRP		58	50.130	19.267	16.967	1.00 40.43	· 6
	MOTA	475		TRP		58	50.427	20.473	17.668	1.00 39.55 1.00 41.08	6
60	MOTA	476	CE2			58	50.354	21.521	16.735	1.00 41.08	6 6
	MOTA	477	CE3	TRP	A	58	50.755	20.770	18.995	1.00 30.30	U

PCT/EP01/01457

WO 01/58951

	11 0 01/302	J1							1 C 1/21 01/014	0,
						-80				
	ATOM	478	CD1	TRP A	. 58	49.887	19.624	15.677	1.00 39.98	6
	MOTA	479	NE1	TRP A	. 58	50.019	20.971	15.527	1.00 41.55	7
	ATOM	480	CZ2	TRP A	. 58	50.599	22.850	17.084	1.00 40.32	6
	ATOM	481		TRP A		50.997	22.081	19.341	1.00 37.03	
5										6
J	ATOM	482	CH2			50.919	23.109	18.389	1.00 38.53	6
	MOTA	483	С	TRP A	. 58	52.112	17.184	16.098	1.00 47.09	· 6
	MOTA	484	0	TRP A	. 58	53.226	17.675	15.915	1.00 47.06	8
	MOTA	485	N	SER A	59	51.390	16.670	15,115	1.00 48.64	7
	ATOM	486	CA	SER A						
10						51.933	16.631	13.782	1.00 50.92	6
10	MOTA	487	CB	SER A		52.245	15.187	13.435	1.00 53.25	6
	MOTA	488	OG	SER A	59	53.191	15.109	12.389	1.00 62.80	8
	MOTA	489	С	SER A	. 59	51.020	17.229	12.735	1.00 52.80	6
	MOTA	490	0	SER A	. 59	49.828	16.942	12.696	1.00 53.05	8
	MOTA.	491	N	ASP A		51.602	18.065			
15	MOTA	492						11.881	1.00 55.45	7
.0			CA	ASP A		50.881	18.72 1	10.792	1.00 57.44	6
	ATOM	493	СВ	ASP A		50.741	20.221	11.071	1.00 57.33	6
	MOTA	494	CG	ASP A	60	49.856	20.936	10.058	1.00 57.43	6
	MOTA	495	OD1	ASP A	60	49.776	20.486	8.896	1.00 57.47	8
	ATOM	496	002	ASP A	60	49.256	21.967	10.424	1.00 56.76	8
20	MOTA	497	C	ASP A						
0						51.726	18.510	9.541	1.00 59.20	6
	MOTA	498	0	ASP A		52.679	19.245	9.304	1.00 58.82	8
	MOTA	499	N	ARG A	61	51.372	17.503	8.748	1.00 61.30	7
	MOTA	500	CA	ARG A	61	52.115	17.181	7.533	1.00 63.09	6
	ATOM	501	СВ	ARG A	61	51.643	15.845	6.958	1.00 67.23	6
25	ATOM	502	CG	ARG A		52.191				
	MOTA						14.594	7.653	1.00 72.92	6
		503	CD	ARG A		51.883	13.355	6.786	1.00 81.01	6
	MOTA	504	NE	ARG A		52.441	12.091	7.291	1.00 85.79	7
	MOTA	505	CZ	ARG A	61	52.320	10.917	6.660	1.00 87.50	6
	ATOM	506	NH1	ARG A	61	51.665	10.843	5.501	1.00 88.31	7
30	MOTA	507		ARG A		52.852	9.815	7.179	1.00 87.74	7
	MOTA	508	C	ARG A						
						52.073	18.238	6.430	1.00 61.94	6
	ATOM	509	0	ARG A	61	52.927	18.225	5.550	1.00 61.39	8
	MOTA	510	N	THR A	62	51.095	19.141	6.461	1.00 60.78	7
	ATOM	511	CA	THR A	62	51.017	20.175	5.434	1.00 59.76	6
35	ATOM	512	CB	THR A	62	49.666	20.952	5.483	1.00 60.01	6
	ATOM	513		THR A	62	49.582	21.720			
								6.689	1.00 62.71	8
	ATOM	514		THR A	62	48.500	20.000	5.442	1.00 59.86	6
	ATOM	515	С	THR A	62	52.172	21.171	5.616	1.00 58.73	6
	MOTA	516	0	THR A	62	52.400	22.044	4.774	1.00 59.33	8
40	ATOM	517	N	LEU A	63	52.898	21.031	6.720	1.00 56.50	7
	MOTA	518	CA	LEU A	63	54.029	21.903	7.020	1.00 55.97	6
	ATOM	519	CB	LEU A	63					
						54.088	22.205	8.521	1.00 53.19	6
	MOTA	520	CG	LEU A	63	52.866	22.837	9.174	1.00 52.76	6
	MOTA	521	CD1	LEU A	63	53.074	22.909	10.672	1.00 51.73	6
45	MOTA	522	CD2	LEU A	63	52.629	24.217	8.589	1.00 53.34	6
	MOTA	523	С	LEU A	63	55.351	21.264	6.603	1.00 55.80	6
	MOTA	524	Ō	LEU A	63	56.366				
							21.947	6.509	1.00 54.36	8
	MOTA	525	N	ALA A	64	55.332	19.952	6.368	1.00 56.30	7
	ATOM	526	CA	ALA A	64	56.532	19.207	5.987	1.00 56.99	6
50	MOTA	527	CB	ALA A	64	56.194	17.744	5.810	1.00 54.20	6
	MOTA	528	С	ALA A	64	57.176	19.745	4.715	1.00 59.20	6
	ATOM	529	0	ALA A	64	56.487	20.224	3.816	1.00 60.08	
	ATOM	530		TRP A						8
			N		65	58.502	19.646	4.651	1.00 60.65	7
EE	ATOM	531	CA	TRP A	65	59.295	20.104	3.506	1.00 62.47	6
55	MOTA	532	CB	TRP A	65	59.623	21.588	3.667	1.00 59.37	6
	MOTA	533	CG	TRP A	65	60.773	21.870	4.613	1.00 56.94	6
	MOTA	534		TRP A	65	60.685	22.167	6.020	1.00 56.89	6
	ATOM	535		TRP A	65	62.001				
							22.424	6.475	1.00 55.08	6
60	MOTA	536		TRP A	65	59.622	22.245	6.938	1.00 54.01	6
60	MOTA	537		TRP A	65	62.097	21.947	4.292	1.00 55.45	6
	MOTA	538	NE1	TRP A	65	62.838	22.282	5.400	1.00 53.98	7

						-81				
	ATOM	539	CZ2	TRP A	65	62.286	22.757	7.808	1.00 52.03	6
	ATOM	540	CZ3	TRP A	65	59.910	22.577	8.266	1.00 53.82	6
	ATOM	541		TRP A	65	61.232	22.829	8.684	1.00 51.71	6
	MOTA	542	C	TRP A	65	60.603	19.297	3.445	1.00 65.72	6
5	ATOM	543	ō	TRP A	65	61.091	18.825	4.479	1.00 66.89	8
_	ATOM	544	N	ASN A	66	61.181	19.138	2.255	1.00 68.69	7
	ATOM	545	CA	ASN A	66	62.431	18.371	2.149	1.00 71.84	6
	ATOM	546	СВ	ASN A	66	62.735	17.983	0.689	1.00 73.23	6
	ATOM	547	CG	ASN A	66	63.968	17.084	0.568	1.00 76.18	6
10	ATOM	548		ASN A	66	64.473	16.822	-0.541	1.00 76.68	8
. •	ATOM	549		ASN A	66	64.463	16.606	1.715	1.00 76.39	7
	ATOM	550	C	ASN A	66	63.581	19.199	2.723	1.00 71.96	6
	MOTA	551	Ō	ASN A	66	63.902	20.279	2.217	1.00 72.02	8
	MOTA	552	N	SER A	67	64.197	18.690	3.784	1.00 72.09	7
15	MOTA	553	CA	SER A	67	65.292	19.403	4.435	1.00 72.65	6
	MOTA	554	СВ	SER A	67	65.063	19.425	5.943	1.00 72.61	6
	ATOM	555	OG	SER A	67	64.969	18.105	6.449	1.00 70.09	8
	ATOM	556	C	SER A	67	66.655	18.794	4.177	1.00 73.27	6
	ATOM	557	0	SER A	67	67.576	19.031	4.961	1.00 72.43	8
20	MOTA	558	N	SER A	68	66.799	18.026	3.097	1.00 74.60	7
	ATOM	559	CA	SER A	68	68.082	17.370	2.825	1.00 76.38	6
	ATOM	560	CB	SER A	68	68.006	16.490	1.564	1.00 75.57	6
	ATOM	561	QG	SER A	68	67.870	17.265	0.386	1.00 75.20	8
	MOTA	562	С	SER A	68	69.222	18.380	2.707	1.00 77.15	6
25	MOTA	563	0	SER A	68	70.288	18.201	3.300	1.00 77.04	8
	ATOM	564	N	HIS A	69	68.992	19.451	1.962	1.00 78.21	7
	ATOM	565	CA	HIS A	69	70.015	20.479	1.804	1.00 79.62	6
	ATOM	566	CB	HIS A	69	70.445	20.578	0.341	1.00 84.04	6
	ATOM	567	CG	HIS A	69	71.007	19.302	-0.196	1.00 88.01	6
30	ATOM	568	CD2	HIS A	69	72.208	19.022	-0.759	1.00 89.20	6
	MOTA	569	ND1	HIS A	69	70.332	18.100	-0.110	1.00 89.31	7
	MOTA	570	CE1	HIS A	69	71.096	17.133	-0.589	1.00 90.18	6
	MOTA	571	NE2	HIS A	69	72.240	17.666	-0.988	1.00 90.99	7
	ATOM	572	С	HIS A	69	69.441	21.799	2.279	1.00 77.78	6
35	MOTA	573	0	HIS A	69	69.473	22.803	1.561	1.00 77.92	8
	ATOM	574	N	SER A	70	68.896	21.766	3.496	1.00 75.27	7
	MOTA	575	CA	SER A	70	68.300	22.931	4.141	1.00 72.21	6
	MOTA	576	CB	SER A	70	67.013	23.316	3.421	1.00 72.74	6
	MOTA	577	OG	SER A	70	66.368	22,158	2.919	1.00 74.05	8
40	MOTA	578	С	SER A	70	68.031	22.563	5.595	1.00 69.35	6
	MOTA	579	0	SER A	70	68.138	21.384	5.962	1.00 70.38	8
	MOTA	580	N	PRO A	71	67.710	23.563	6.450	1.00 66.44	7
	MOTA	581	CD	PRO A	71	67.819	24.998	6.134	1.00 64.03	6
	MOTA	582	CA	PRO A	71	67.422	23.385	7.883	1.00 64.80	6 6
45	MOTA	583	CB	PRO A	71	67.106	24.805	8.334	1.00 63.49	
	MOTA	584	CG	PRO A		68.031		7.498		6
	MOTA	585	С	PRO A		66.295	22.395	8.223	1.00 63.99	6
	MOTA	586	0	PRO A		65.314	22.289	7.496	1.00 63.63	8
	MOTA	587	N	ASP A		66.434	21.679	9.333	1.00 63.39	7
50	MOTA	588	CA	ASP A		65.424	20.701	9.734	1.00 63.43	6
	MOTA	589	CB	ASP A		66.056	19.634	10.617	1.00 65.69	6
	MOTA	590		ASP A		67.229	18.974	9.959	1.00 70.53	6
	MOTA	591		L ASP A		66.985	18.216	8.988	1.00 73.68 1.00 71.00	8 8
	MOTA	592		2 ASP A		68.389		10.390		6
55	ATOM	593		ASP A		64.307	21.356	10.520	1.00 62.20 1.00 61.88	8
	MOTA	594		ASP A		63.164	20.878	10.520	1.00 51.88	7
	MOTA	595		GLN A		64.653	22.457	11.175	1.00 59.85	6
	MOTA	596				63.738	23.186	12.041	1.00 59.45	6
60	MOTA	597			_	64.083	22.901	13.489 14.035	1.00 63.59	6
60	MOTA	598				63.720	21.569	15.459	1.00 68.15	6
	MOTA	599	CD	GLN A	. 73	64.224	21.462	15.459	1.00 00.15	U

PCT/EP01/01457

							-82				
	ATOM	600	OE1	GLN Z	Δ	73	65.425	21.595	15.699	1.00 70.61	8
	ATOM	601		GLN A		73	63.316	21.249	16.416	1.00 69.73	7
	ATOM	602	C	GLN A		73	63.779	24.703	11.886	1.00 57.04	6
	ATOM	603	ō	GLN 3		73	64.798	25.280	11.490	1.00 58.19	8
5	ATOM	604	N	VAL 2		74	62.670	25.336	12.243	1.00 52.68	7.
	MOTA	605	CA	VAL .		74	62.557	26.782	12.211	1.00 50.24	6
	MOTA	606	СВ	VAL .		74	62.036	27.279	10.859	1.00 48.70	6
	MOTA	607	CG1	VAL .	A	74	63.066	27.034	9.794	1.00 49.74	6
	MOTA	608	CG2	VAL .	A	74	60.738	26.584	10.515	1.00 47.98	6
10	MOTA	609	С	VAL .		74	61.580	27.201	13.310	1.00 49.74	6
	MOTA	610	0	VAL .	A	74	60.756	26.401	13.754	1.00 48.96	8
	MOTA	611	N	SER .		75	61.691	28.442	13.769	1.00 47.62	7
	MOTA	612	CA	SER		75	60.792	28.954	14.787	1.00 44.06	6 6
45	MOTA	613	CB	SER		75	61.525	29.902	15.728	1.00 44.67	8
15	MOTA	614	OG	SER		75	62.241	29.188	16.710	1.00 46.37	6
	MOTA	615	C	SER		75	59.668	29.688	14.084	1.00 43.07 1.00 42.11	8
	MOTA	616	0	SER		75	59.894	30.657	13.358	1.00 42.11	7
	MOTA	617	N	VAL		76	58.451 57.272	29.214 29.792	14.307 13.687	1.00 42.71	6
00	MOTA	618	CA	VAL		76 76		28.711	12.936	1.00 44.34	6
20	MOTA	619	CB CC1	VAL		76 76	56.482 55.247	29.315	12.298	1.00 44.97	6
	ATOM	620		VAL VAL		76 76	57.359	28.058	11.894	1.00 43.12	6
	ATOM	621 622	CGZ	VAL		76	56.335	30.436	14.704	1.00 44.16	6
	MOTA	623	0	VAL		76	56.093	29.882	15.773	1.00 45.89	8
25	ATOM ATOM	624	Ŋ	PRO		77	55.798	31.624	14.388	1.00 43.19	7
23	ATOM	625	CD	PRO		77	56.162	32.556	13.311	1.00 41.24	6
	ATOM	626	CA	PRO		77	54.884	32.266	15.334	1.00 41.49	6
	ATOM	627	CB	PRO		77	54.619	33.615	14.691	1.00 41.13	6
	ATOM	628	CG	PRO		77	55.886	33.884	13.950	1.00 41.89	6
30	ATOM	629	C	PRO		77	53.617	31.439	15.453	1.00 40.82	6
00	ATOM	630	ŏ	PRO		77	53.112	30.919	14.471	1.00 39.55	8
	ATOM	631	N	ILE		78	53.116	31.318	16.671	1.00 42.42	7
	ATOM	632	CA	ILE		78	51.908	30.556	16.959	1.00 42.14	6
	ATOM	633	CB	ILE	Α	78	51.526	30.751	18.441	1.00 42.09	6
35	ATOM	634	CG2	ILE	Α	78	50.105	30.357	18.712	1.00 43.53	6
	ATOM	635	CG1	ILE	Α	78	52.464	29.921	19.285	1.00 43.22	6
	MOTA	636	CD1	ILE	A	78	52.585	28.513	18.784	1.00 43.92	6
	ATOM	637	Ç	ILE	Α	78	50.749	30.942	16.057	1.00 43.58	6
	MOTA	638	0	ILE		78	49.985	30.096	15.624	1.00 45.64	8
40	MOTA:	639	N	SER		79	50.642	32.229	15.768	1.00 43.79	7 6
	ATOM	640	CA	SER		79	49.588	32.767	14.918	1.00 44.38 1.00 44.81	6
	MOTA	641	CB	SER		79	49.666	34.292	14.934	1.00 45.88	8
	MOTA	642	OG	SER		79	50.972	34.732 32.295	14.584 13.465	1.00 43.50	6
4 =	MOTA	643	C	SER SER		79 79	49.590 48.607	32.498	12.758	1.00 42.80	8
45	MOTA	644	O	SER		80	50.685	31.683	13.016	1.00 42.62	7
	MOTA MOTA	645 646	N CA	SER		80	50.774	31.216	11.639	1.00 42.84	6
	ATOM	647	CB	SER		80	52.137	31.555	11.043	1.00 44.68	6
	ATOM	648	OG	SER		80	52.308	32.956	10.932	1.00 51.59	8
50	MOTA	649	C	SER		80	50.534	29.726	11.502	1.00 44.69	6
00	MOTA	650	o	SER		80	50.596	29.184	10.402	1.00 43.97	8
	MOTA	651		LEU		81	50.248	29.068	12.620	1.00 45.13	7
	MOTA	652	CA	LEU		81	50.003	27.631	12.631	1.00 41.19	6
	MOTA		·CB	LEU		81	51.061	26.926	13.467	1.00 39.92	6
55	ATOM	654	CG	LEU		81	52.534	27.167	13.185	1.00 41.52	6
	MOTA	655		LEU		81	53.356	26.677	14.355	1.00 39.70	6
	MOTA	656		2 LEU		81	52.922	26.464	11.918	1.00 42.52	6
	MOTA	657		LEU	Α	81	48.672	27.340	13.272	1.00 39.47	6
	MOTA	658		LEU	Α	81	48.089	28.197	13.921	1.00 40.21	8
60	MOTA	659	N	TRP	Α	82	48.191	26.122	13.081	1.00 38.46	7
	MOTA	660	CA	TRP	A	82	46.965	25.694	13.720	1.00 37.32	6

	WO 01/589	951								PCT/EP01/01457	
							-83				
	MOTA	661	СВ	TRP	λ.	82	46.346	24.494	13.006	1.00 36.83	6
	MOTA	662	CG	TRP		82	45.274	23.818	13.829		6
	ATOM	663		TRP		82	45.459	22.741	14.757		6
	MOTA	664		TRP		82	44.213	22.499	15.369		6
5	MOTA	665		TRP		82	46.560	21.961	15.132	1.00 40.54	6
	MOTA	666		TRP		82	43.948	24.170	13.914		6
	MOTA	667		TRP		82	43.311	23.383	14.839		7
	MOTA	668	CZ2	TRP		82	44.040	21.511	16.332		6
10	MOTA	669		TRP		82	46.388	20.982	16.088		6
10	ATOM	670	CH2	TRP		82 82	45.135	20.764 25.241	16.678		6 6
	ATOM ATOM	671 672	C O	TRP TRP		82	47.485 48.559	24.661	15.064 15.142		8
	MOTA	673	N	VAL		83	46.744	25.503	16.123		7
	ATOM	674	CA	VAL		83	47.179	25.086	17.437		6
15	MOTA	675	СВ	VAL		83	47.729	26.300	18.209		6
	MOTA	676	CG1	VAL	A	83	47.901	25.984	19.655	1.00 43.51	6
	MOTA	677	CG2	VAL	Α	83	49.054	26.688	17.644	1.00 37.34	6
	MOTA	678	С	VAL	A	83	46.011	24.437	18.175	1.00 39.74	6
00	MOTA	679	0	VAL		83	44.858	24.823	17.997		8
20	ATOM	680	N	PRO		84	46.290	23.408	18.982		7
	MOTA	681	CD	PRO		84	47.594	22.745	19.134		6
	ATOM ATOM	682 683	CA CB	PRO PRO		84	45.263 46.079	22.701 21.690	19.752 20.558		6
	ATOM	684	CG	PRO		84 84	47.202	21.390	19.663		6 6
25	ATOM	685	C	PRO		84	44.509	23.663	20.658		6
	MOTA	686	ŏ	PRO		84	45.121	24.469	21.342		8
	ATOM	687	N	ASP		85	43.186	23.576	20.668		7
	ATOM	688	CA	ASP	Α	85	42.397	24.458	21.505	1.00 34.36	6
	MOTA	689	СВ	ASP		85	41.014	24.668	20.898		6
30	MOTA	690	CG	ASP		85 ·	40.268	23.381	20.696	1.00 37.78	б
	MOTA	691		ASP		85	40.897	22.388	20.290		8
	ATOM	692		ASP		85	39.050	23.367	20.927		8
	MOTA	693	C	ASP		85	42.277	23.906	22.910		6
35	MOTA MOTA	694 695	N O	ASP LEU		85 86	41.180	23.726 23.644	23.420 23.528		8 7
-	ATOM	696	CA	LEU		86	43.459	23.106	24.869		, 6
	ATOM	697	CB	LEU		86	44.878	22.670	25.208		6
	MOTA	698	CG	LEU		86	45.435	21.585	24.311		6
	ATOM	699	CD1	LEU	Α	86	46.842	21.241	24.749	1.00 34.84	б
40	MOTA	700		LEU	A	86	44.530	20.376	24.386	1.00 35.68	6
	MOTA	701	С	LEU		86	42.973	24.086	25.925		6
	MOTA	702	0	LEU		86	43.141	25.283	25.800		8
	MOTA	703	N	ALA		87	42.378	23.556	26.979		7
45	MOTA MOTA	704 705	CA CB	ALA ALA		87 87	41.870 40.428	24.369	28.060		6
70	ATOM	705	C	ALA		87	42.022	24.674 23.605	27.811		6 6
	ATOM	707	ō	ALA		87	41.798	22.399	29.407		8
	ATOM	708	N	ALA		88	42.431	24.290	30.436		7
	MOTA	709	CA	ALA	Α	88	42.558	23.639	31.726		6
50	MOTA	710	CB	ALA	Α	88	43.586	24.337	32.571		6
	MOTA	711	С	ALA	Α	88	41.180	23.729	32.376		6
	MOTA	712	0	ALA		88	40.778	24.780	32.847		8
	ATOM	713	N	TYR		89	40.460	22.613	32.371		7
55	MOTA	714	CA	TYR		89	39.116	22.502	32.934		6
33	ATOM	715 716	CB	TYR		89 aa	38.727	21.023	33.052		6
	MOTA MOTA	716 717	CG CD1	TYR TYR		89 89	38.641 38.462	20.286 18.902	31.725 31.684		6 6
	ATOM	718		TYR		89	38.353	18.222	30.466		6
	ATOM	719		TYR		89	38.711	20.968	30.511		6
60	ATOM	720		TYR		89	38.604	20.297	29.302		6
	MOTA	721	CZ	TYR		89	38.424	18.927	29.286		6
										•	

							-84				
	ATOM	722	OH	TYR .	Α	89	38.296	18.257	28.093	1.00 59.35	8
	ATOM	723	C	TYR		89	38.888	23.185	34.280	1.00 43.81	6
	ATOM	724	0	TYR		89	37.808	23.735	34.518	1.00 41.70	8
	ATOM	725		ASN		90	39.880	23.149	35.167	1.00 43.90	7
5	ATOM	726		ASN		90	39.709	23.781	36.473	1.00 43.12	6
J	ATOM	727	СВ	ASN		90	39.976	22.770	37.598	1.00 40.92	6
	ATOM	728	CG	ASN		90	41.340	22.156	37.517	1.00 42.04	6
	MOTA	729		ASN		90	41.770	21.721	36.456	1.00 43.62	8
	ATOM	730		ASN		90	42.033	22.102	38.646	1.00 43.25	7
10	ATOM	731	C	ASN		90	40.550	25.042	36.655	1.00 44.35	6
. •	MOTA	732	ō	ASN		90	40.881	25.434	37.769	1.00 46.42	8
	ATOM	733	N	ALA		91	40.902	25.673	35.543	1.00 45.44	7
	ATOM	734	CA	ALA		91	41.660	26.912	35.591	1.00 45.36	6
	ATOM	735	СВ	ALA	Α	91	42.130	27.308	34.206	1.00 44.43	6
15	MOTA	736	c	ALA		91	40.680	27.940	36.136	1.00 45.00	6
. –	MOTA	737	Ō	ALA		91	39.522	28.000	35.729	1.00 43.71	8
	ATOM	738	N	ILE		92	41.164	28.750	37.064	1.00 46.47	7
	ATOM	739	CA	ILE	Α	92	40.359	29.753	37.734	1.00 46.18	6
	ATOM	740	CB	ILE	Α	92	40.674	29.673	39.232	1.00 47.56	6
20	MOTA	741	CG2	ILE	А	92	41.595	30.797	39.634	1.00 50.92	6
	ATOM	742	CG1	ILE	Α	92	39.409	29.713	40.055	1.00 50.52	6
	ATOM	743	CD1	ILE	Α	92	39.711	29.795	41.547	1.00 51.82	6
	ATOM	744	С	ILE	Α	92	40.659	31.157	37.177	1.00 45.80	6
	MOTA	745	0	ILE	Α	92	39.996	32.134	37.518	1.00 45.79	8
25	ATOM	746	N	SER	A	93	41.666	31.237	36.317	1.00 44.40	7
	MOTA	747	CA	SER	А	93	42.076	32.483	35.687	1.00 41.89	6
	MOTA	748	CB	SER	Α	93	43.248	33.080	36.445	1.00 40.83	6
	MOTA	749	OG	SER	Α	93	44.400	32.275	36.274	1.00 37.97	8
	MOTA	750	С	SER		93	42.541	32.112	34.295	1.00 42.18	6
30	MOTA	751	0	SER	Α	93	42.762	30.942	34.023	1.00 41.06	8
	MOTA	752	И	LYS		94	42.693	33.081	33.401	1.00 43.27	7
	MOTA	753	CA	LYS		94	43.178	32.712	32.077	1.00 45.47	6
	MOTA	754	CB	LYS		94	42.703	33.680	30.988	1.00 44.26	6
0-	MOTA	755	CG	LYS		94	42.747	35.142	31.314	1.00 44.49	6
35	MOTA	756	CD	LYS		94	41.907	35.918	30.309	1.00 46.66	6
	ATOM	757	CE	LYS		94	42.209	35.470	28.885	1.00 47.75	6 7
	MOTA	758	NZ	LYS		94	41.443	36.237	27.873	1.00 49.19	6
	MOTA	759	C	LYS		94	44.688 45.359	32.592	32.089 32.980	1.00 43.67 1.00 44.46	8
40	MOTA	760	0	LYS		94	45.339	33.102 31.889	31.105	1.00 43.23	7
40	MOTA	761	N	PRO		95 95	44.559	31.199	30.004	1.00 43.23	6
	MOTA	762	CD	PRO		95	46.692	31.695	31.024	1.00 42.80	6
	MOTA MOTA	763 764	CA CB	PRO PRO		95	46.858	30.719	29.862	1.00 43.77	6
	ATOM	765	CG	PRO		95	45.515	30.723	29.725	1.00 43.00	6
45	MOTA	766	C	PRO		95	47.480	32.962	30.783	1.00 41.84	6
40	MOTA	767	0	PRO		95	47.178	33.729	29.861	1.00 41.82	8
	ATOM	768	N	GLU		96	48.483	33.183	31.627	1.00 40.74	7
	MOTA	769	CA	GLU		96	49.350	34.322	31.472	1.00 39.25	6
	MOTA	770	CB	GLU		96	49.704	34.960	32.817	1.00 41.50	6
50	ATOM	771	CG	GLU		96	50.548	36.235	32.682	1.00 46.46	6
	ATOM	772	CD	GLU		96	50.864	36.910	34.014	1.00 51.10	6
	ATOM	773		GLU		96	50.172	36.591	35.002	1.00 55.39	8
	MOTA	774		GLU		96	51.784	37.772	34.079	1.00 51.01	8
	MOTA	775	С	GLU		96	50.583	33.713	30.851	1.00 38.30	6
55	MOTA	776	0	GLU	Α	96	51.424	33.169	31.548	1.00 37.33	8
	ATOM	777	N	VAL		97	50.662	33.770	29.528	1.00 36.80	7
	MOTA	778	CA	VAL	Α	97	51.813	33.231	28.821	1.00 37.13	6
	ATOM	779	CB	VAL	A	97	51.514	33.092	27.313	1.00 35.99	6
	MOTA	780	CG1	VAL	Α	97	52.704	32.480	26.600	1.00 34.96	6
60	MOTA	781	CG2	VAL		97	50.287	32.222	27.122	1.00 30.36	6
	MOTA	782	С	VAL	A	97	53.002	34.160	29.061	1.00 37.37	6

						-85					
	ATOM	783	0	VAL A	97	52.998	35.329	28.670	1.00 3		8
	ATOM	784		LEU A	98	54.022	33.619	29.715	1.00 3		7
	ATOM	785		LEU A	98	55.203	34.389	30.070	1.00 3		6
	ATOM	786	СВ	LEU A	98		33.851	31.374	1.00 3		6
5	MOTA	787	CG	LEU A	98		33.662	32.568	1.00 3		. 6
	ATOM	788	CD1	LEU A	98	55.522	32.772	33.576	1.00 3		· 6
	ATOM	789	CD2	LEU A	98		34.997	33.169	1.00	38.93 41 70	6 6
	MOTA	790		LEU A	98		34.387	29.033	1.00 4		8
	MOTA	791		LEU A	98	57.310	35.114	29.177 27.992	1.00 4		7
10	MOTA	792		THR A	99	56.162	33.579 33.471	26.981	1.00		6
	MOTA	793	CA	THR A	99	57.199 57.793	32.063	27.004	1.00		6
	MOTA	794	CB	THR A	99 99	56.745	31.102	26.822	1.00		8
	MOTA	795		THR A	99	58.490	31.812	28.325	1.00		6
45	ATOM	796	CG2 C	THR A	99	56.762	33.784	25.559	1.00		6
15	MOTA	797 798	0	THR A	99	55.571	33.809	25.260	1.00		8
	ATOM ATOM	799	N	PRO A		57.733	34.050	24.666	1.00	35.48	7
	ATOM	800	CD	PRO A		59.169	34.217	24.938	1.00	34.88	6
	ATOM	801	CA	PRO A		57.450	34.356	23.268	1.00		6
20	ATOM	802	СВ	PRO A		58.825	34.308	22.631	1.00		6
_•	ATOM	803	CG	PRO A	100	59.660	34.899	23.674	1.00		6
	ATOM	804	С	PRO A	100	56.535	33.287	22.735		34.32	6
	MOTA	805	0	PRO A	100	56.748	32.110	22.990		37.05	8
	MOTA	806	N	GLN A	101	55.508	33.684	22.005		35.52	7
25	MOTA	807	CA	GLN A	101	54.591	32.698	21.483		38.08	6 6
	MOTA	808	CB	GLN A		53.181	33.271	21.452		39.02	6
	MOTA	809	CG	GLN A		52.557	33.223	22.836 22.965		42.77 46.68	6
	MOTA	810	CD	GLN A		51.356	34.102 33.943	22.239		51.63	8
-00	MOTA	811		GLN A		.50.383	35.045	23.900		48.84	7
30	MOTA	812		GLN A		51.408 55.006	32.145	20.144		37.60	6
	MOTA	813	С	GLN A		54.331	32.329	19.136		36.16	8
	ATOM	814 815	N O	LEU A		56.138	31.445	20.177		38.73	7
	ATOM ATOM	816	CA	LEU A		56.742	30.812	19.016	1.00	38.35	6
35	MOTA	817	CB	LEU A		58.180	31.289	18.833	1.00	36.63	6
00	ATOM	818	CG	LEU A		58.411	32.792	18.709	1.00	37.99	6
	ATOM	819		LEU A		59.890	33.054	18.550		39.54	6
	ATOM	820		LEU A		57.650	33.343	17.538		35.40	6
	MOTA	821	С	LEU A	102	56.763	29.311	19.200		39.23	6
40	ATOM	822	0	LEU A		56.933	28.809	20.302		40.34	8
	MOTA	823	N	ALA A		56.574	28.595	18.104		40.83	7 6
	MOTA	824	CA	ALA A		56.603	27.142	18.125		41.49 41.49	6
	MOTA	825	CB	ALA A		55.334	26.569	17.497 17.337		42.17	6
4.5	ATOM.	826	C	ALA A		57.830	26.697 27.484	16.645		43.45	8
45	ATOM	827		ALA A		58.472 58.163	25.427	17.453			7
	MOTA	828	N	ARG A		59.309	24.893	16.750	1.00	44.63	6
	MOTA	829		ARG A		60.242	24.228	17.745	1.00	43.89	6
	MOTA	830 831		ARG A		61.621	23.992	17.214		45.78	6
50	ATOM ATOM	832			104	62.362	25.277	16.950		43.65	6
50	ATOM	833		ARG 2		63.675	24.958	16.409		44.01	7
	ATOM	834			A 104	64.618	25.848	16.124		46.53	6
	ATOM	835		ARG A		.64.411	27.147	16.327		47.99	7
	ATOM	836		ARG		65.775	25.432	15.632		47.13	7
55	MOTA	837			A 104	58.770	23.878	15.754		46.81	6
	MOTA	838		ARG A	A 104	58.042	22.961	16.124		49.12	8
	MOTA	839	N		A 105	59.097	24.049	14.482		47.69	7
	MOTA	840			A 105	58.601	23.125	13.469		47.16 44.84	6 6
	MOTA	841			A 105	57.791	23.857	12.382		41.16	6
60		842		1 VAL		57.198	22.861	11.421 13.018		45.42	6
	MOTA	843	G CG	2 VAL .	A 105	56.702	24.684	13.018	1.00	43.42	J

	WO 01/5895	51								PCT/	EP01/014	57
							-86					
	MOTA	844	С			105	59.731	22.355	12.799		49.71	6
	MOTA	845	0	VAL			60.688	22.946	12.283		48.12	8
	MOTA	846	N	VAL			59.597	21.030	12.821		50.55	7
5	MOTA MOTA	847 848	CA CB	VAL		106	60.571 60.648	20.123	12.232		51.43	6
9	MOTA	849		VAL			61.828	18.816 17.987	13.037 12.571		52.44 50.24	6 6
	ATOM	850		VAL			60.762	19.128	14.521		52.53	6
	ATOM	851	C			106	60.142	19.809	10.805		52.38	6
	ATOM	852	Ö			106	58.961	19.644	10.536		52.65	8
10	MOTA	853	N	SER	Α	107	61.101	19.718	9.895		52.34	7
	ATOM	854	CA	SER	Α	107	60.803	19.447	8.492	1.00	54.32	6
	MOTA	855	CB			107	62.111	19.185	7.735	1.00	55.62	6
	ATOM	856	OG			107	62.965	18.316	8.462		60.14	8
15	MOTA	857	, C			107	59.795	18.328	8.186		53.69	6
15	MOTA	858	0			107	59.191	18.304	7.111		51.90	8
	MOTA MOTA	859 860	N CA	ASP		108	59.598 58.667	17.412 16.318	9.122 8.890		54.61 57.15	7
	ATOM	861	CB	ASP			59.164	15.046	9.580		58.72	6 6
	ATOM	862	CG	ASP			59.114	15.134	11.097		61.68	6
20	ATOM	863		ASP			59.391	16.221	11.642		64.28	8
	MOTA	864		ASP			58.816	14.105	11.747		62.23	8
	MOTA	865	С	ASP	Α	108	57.235	16.615	9.320	1.00	58.57	6
	MOTA	866	0	ASP			56.379	15.725	9.301	1.00	58.30	8
٥٢	ATOM	867	N	GLY			56.979	17.865	9.703		59.1 4	7
25	MOTA	868	CA			109	55.649	18.271	10.116		58.25	6
	ATOM	869	C	GLY			55.397	18.166	11.602		58.69	6
	ATOM ATOM	870 871	N O	GLY GLY			54.273 56.423	18.374 17.821	12.054 12.369		59.98 58.71	8
	ATOM	872	CA	GLU			56.255	17.713	13.813		58.33	7 6
30	ATOM	873	CB			110	57.380	16.871	14.425		61.59	6
	MOTA	874	CG	GLU			57.062	16.242	15.797		66.10	6
	MOTA	875	CD	GLU			55.913	15.218	15.728		70.89	6
	ATOM	876	OE1	GLU	A	110	55.634	14.710	14.600	1.00	70.53	8
0.5	ATOM	877	OE2				55.303	14.916	16.800		70.77	8
35	ATOM	878	С			110		19.136	14.369		56.59	6
	MOTA	879	0	GLU			57.114	19.955	13.941		54.81	8
	MOTA MOTA	880 881	N CA	VAT VAT			55.392 55.310	19.425	15.307		54.27	7
	MOTA	882	CB	VAL			53.949	20.745 21.412	15.912 15.616		52.01 50.79	6 6
40	ATOM	883		VAL			53.902	22.795	16.242		47.90	6
_	MOTA	884		VAL			53.718	21.489	14.115		50.80	6
	MOTA	885	С	VAL			55.465	20.666	17.418		51,33	6
	MOTA	886	0	VAL	Α	111	54.833	19.830	18.057	1.00	50.54	8
4.5	MOTA	887	N	LEU			56.300	21.539	17.979	1.00	49.64	7
45	ATOM	888	CA	LEU			56.501	21.569	19.418		50.36	6
	ATOM	889	CB	LEU			57.911	21.107	19.791		54.86	6
	ATOM ATOM	890 891	CG CD1	LEU			58.651 57.699	20.020	18.989		59.01	6
	ATOM	892		LEU			59.248	18.865 20.632	18.631 17.727		60.90 57.28	6
50	ATOM	893	C	LEU			56.297	22.980	19.946		49.94	6 6
	ATOM	894	ō	LEU			57.004	23,893	19.553		49.38	8
	MOTA	895	N	TYR			55.323	23.151	20.833		49.46	7
	ATOM	896	CA	TYR			55.036	24.446	21.437		47.23	6
	MOTA	897	CB	TYR			53.643	24.939	21.021		45.72	6
55	ATOM	898	CG	TYR			53.222	26.279	21.621		46.02	6
	ATOM	899	. CD1				54.092	27.364	21.654		42.86	6
	MOTA	900		TYR			53.691	28.588	22.179		43.03	6
	MOTA MOTA	901 902	CD2	TYR TYR			51.936 51.533	26.462	22.131 22.653		45.25	6
60	MOTA	903	CEZ	TYR			52.410	27.682 28.740	22.633		41.00 42.42	6 6
	ATOM	904	OH	TYR			52.008	29.952	23.211		42.79	8
							· -					-

						-87				
	MOTA	905	С	TYR A	113	55.097	24.250	22.936	1.00 47.38	6
	MOTA	906	0	TYR A	113	54.304	23.508	23.506	1.00 47.08	8
	ATOM	907	N	MET A	114	56.047	24.916	23.577	1.00 48.38	7
	MOTA	908	CA	MET A	114	56.205	24.788	25.015	1.00 48.39	6
5	MOTA	909	СВ	MET A	114	57.485	24.020	25.304	1.00 52.09	_. 6
	MOTA	910	CG	MET A		57.675	23.679	26.739	1.00 59.10	6
	MOTA	911	SD	MET A		59.383	23.282	26.925	1.00 67.20	16
	ATOM	912	CE	MET A		59.324	21.518	26.416	1.00 67.26	6
40	MOTA	913	С	MET A		56.245	26.148	25.701	1.00 46.12	6
10	MOTA	914	0	MET A		57.308	26.660	26.027	1.00 46.76	8 7
	MOTA	915	N	PRO A		55.076	26.754 26.329	25.922 25.463	1.00 44.80 1.00 44.54	6
	ATOM ATOM	916 917	CD CA	PRO A		53.740 55.005	28.059	26.575	1.00 44.34	6
	ATOM	918	CB	PRO A		53.675	28.598	26.075	1.00 45.01	6
15	ATOM	919	CG	PRO A		52.831	27.366	26.077	1.00 43.44	6
. •	ATOM	920	C	PRO A		55.030	27.935	28.102	1.00 43.24	6
	ATOM	921	Ö	PRO A		54.552	26.947	28.664	1.00 40.79	8
	ATOM	922	N	SER A		55.599	28.929	28.771	1.00 42.36	7
	ATOM	923	CA	SER A		55.627	28.911	30.227	1.00 42.64	6
20	ATOM	924	CB	SER A	116	56.851	29.624	30.764	1.00 40.99	6
	MOTA	925	OG	SER A	116	56.852	29.573	32.169	1.00 41.56	8
	ATOM	926	С	SER A	116	54.382	29.658	30.653	1.00 42.71	6
	MOTA	927	0	SER A		54.184	30.809	30.266	1.00 44.52	8
05	ATOM	928	N	ILE A		53.545	29.006	31.446	1.00 41.18	7
25	ATOM	929	CA	ILE A		52.303	29.616	31.879	1.00 40.12	6
	ATOM	930	CB	ILE A		51.104	28.814	31.325	1.00 37.67	6 6
	ATOM ATOM	931 932	CG2			49.805 51.134	29.400 28.825	31.819 29.798	1.00 38.25 1.00 36.76	6
	ATOM	933	CD1	ILE A		50.212	27.822	29.169	1.00 33.48	6
30	ATOM	934	CDI	ILE A		52.114	29.768	33.388	1.00 41.31	6
00	ATOM	935	ō	ILE A		52.444	28.876	34.168	1.00 43.78	8
	ATOM	936	N	ARG A		51.607	30.925	33.795	1.00 41.35	7
	ATOM	937	CA	ARG A		51.283	31.153	35.194	1.00 41.26	6
	MOTA	938	CB	ARG A	118	51.789	32.496	35.709	1.00 38.56	6
35	MOTA	939	CG	ARG A	118	51.290	32.758	37.113	1.00 37.29	6
	MOTA	940	CD	ARG A	118	52.006	33.883	37.817	1.00 38.24	6
	ATOM	941	NE	ARG A		51.453	34.066	39.150	1.00 41.49	7
	MOTA	942	CZ	ARG A		52.006	34.794	40.107	1.00 43.10	6
40	ATOM	943		ARG A		53.148	35.423	39.892	1.00 46.98	7
40	ATOM	944		ARG A		51.417	34.890	41.282	1.00 43.21	7
	MOTA	945	C	ARG A		49.765	31.156	35.179	1.00 41.21	6
	MOTA MOTA	946 947	N O	ARG A GLN A		49.144 49.152	31.8 4 2 30.394	34.374 36.063	1.00 41.57 1.00 41.94	8 7
	MOTA	948	CA	GLN A		47.702	30.329	36.056	1.00 43.44	6
45	ATOM	949	CB	GLN A		47.702	29.433	34.895	1.00 41.21	6
	ATOM	950	CG	GLN A		45.825	29.257	34.672	1.00 43.47	6
	ATOM	951	CD	GLN . A		45.552	28.554	33.364	1.00 41.25	6
	MOTA	952	OE1			46.333	27.721	32.931	1.00 42.28	8
	MOTA	953	NE2	GLN A	119	44.439	28.877	32.736	1.00 42.81	7
50	MOTA	954	С	GLN A	119	47.183	29.801	37.385	1.00 44.09	6
	MOTA	955	0	GLN A	119	47.866	29.041	38.062	1.00 43.59	8
	MOTA	956	N	ARG A		45.990	30.228	37.778	1.00 46.26	7
	MOTA	957	CA	ARG A		45.433	29.762	39.036	1.00 48.60	6
EE.	MOTA	958	CB	ARG A		44.780	30.900	39.797	1.00 51.27	6
55·	MOTA	959	CG	ARG A		45.705	32.036	40.096	1.00 60.62	6
	MOTA	960	CD	ARG A		45.261	32.728	41.362	1.00 67.20 1.00 69.70	6
	MOTA MOTA	961 962	NE CZ	ARG A		45.730 44.989	32.045 31.859	42.575 43.668	1.00 69.76	7 6
	ATOM	963		ARG A		43.728	32.279	43.709	1.00 68.36	
60	MOTA	964		ARG A		45.533	31.307	44.748	1.00 70.33	7
	ATOM	965	C	ARG A		44.414	28.669	38.804	1.00 48.02	6
	· -					· = -				

					-88				
	» mow	966 (O ARGA	120	43.706	28.669	37.788	1.00 46.40	8
	MOTA		N PHE A		44.341		39.753	1.00 46.74	7
	ATOM ATOM		CA PHE A		43.406	26.628	39.648	1.00 48.15	6
	ATOM		CB PHE A		44.129	25.330	39.301	1.00 45.72	6
5	ATOM		CG PHE A		44.973	25.415	38.074	1.00 44.95	6
•	ATOM		CD1 PHE A		46.240	25.993	38.122	1.00 43.54	·6 6
	ATOM		CD2 PHE A		44.495	24.944	36.866	1.00 41.66	6
	ATOM		CE1 PHE A		47.011	26.099	36.986	1.00 42.05	6
	ATOM	974	CE2 PHE A	121	45.257	25.047	35.733	1.00 41.56 1.00 42.24	6
10	MOTA	975	CZ PHE A		46.521	25.628	35.790	1.00 42.24	6
•	MOTA	976	C PHE A		42.622	26.376	40.908	1.00 49.47	8
	MOTA	977	O PHE A		42.996	26.810	42.001 40.727	1.00 51.17	7
•	MOTA	978	N SER A		41.524	25.653	41.823	1.00 52.06	6
	MOTA	979	CA SER A		40.657	25.250 25.501	41.477	1.00 52.69	6
15	MOTA	980	CB SER A		39.193 38.354	25.046	42.520	1.00 51.12	8
	MOTA	981	OG SER A		40.896	23.754	41.978	1.00 52.70	6
	ATOM	982	C SER A O SER A		40.529	22.966	41.103	1.00 51.13	8
	MOTA	983			41.543	23.369	43.070	1.00 52.97	7
20	MOTA	984	N CYS A		41.820	21.967	43.312	1.00 56.03	6
20	MOTA	985 986	C CYS A		42.017	21.693	44.803	1.00 59.48	6
	MOTA	987	O CYS A		41.882	22.602	45.634	1.00 60.13	8
	MOTA MOTA	988	CB CYS A		43.052	21.555	42.534	1.00 53.78	6
	MOTA	989	SG CYS A		44.483	22.558	42.968	1.00 56.89	16
25	ATOM	990	N ASP A		42.342	20.443	45.143	1.00 61.91	7
	MOTA	991	CA ASP A		42.525	20.084	46.542	1.00 63.81	6
	ATOM	992	CB ASP A	124	42.391	18.571	46.749	1.00 65.05	6
	MOTA	993	CG ASP A		41.828	18.226	48.128	1.00 66.74	6 8
	MOTA	994	OD1 ASP A		42.113	18.973	49.103	1.00 65.03 1.00 67.39	8
30	MOTA	995	OD2 ASP A		41.101	17.209	48.234	1.00 63.72	6
	MOTA	996	C ASP A		43.857	20.543	47.110 46.745	1.00 63.72	8
	MOTA	997	O ASP A		44.910	20.036	48.031	1.00 64.49	7
	MOTA	998	N VAL A		43.794	21.495 22.042	48.681	1.00 63.28	6
	MOTA	999	CA VAL A		44.981 44.861	23.578	48.804	1.00 62.29	6
35	MOTA	1000	CB VAL A		46.058	24.135	49.539	1.00 61.76	6
	MOTA	1001	CG1 VAL A		44.735		47.429	1.00 61.51	6
	MOTA	1002	CG2 VAL A		45.190		50.078	1.00 63.42	6
	MOTA	1003			46.283		50.632	1.00 63.08	8
40	MOTA	1004 1005	O VAL A		44.141		50.641	1.00 64.34	7
40	MOTA	1005	CA SER		44.218		51.981	1.00 64.43	6
	MOTA MOTA	1000	CB SER F		42.924		52.302	1.00 63.15	6
	MOTA	1008	OG SER A		42.723	18.465	51.371		8
	MOTA	1009	C SER		45.414		52.128	1.00 64.40	6
45	ATOM	1010		A 126	45.636	18.420	51.299		8
	ATOM	1011	N GLY	A 127	46.188		53.186		7
	MOTA	1012	CA GLY	A 127	47.343				6 6
	ATOM	1013	C GLY	A 127	48.647				8
	MOTA	1014	O GLY	A 127	49.725				7
50	MOTA	1015		A 128	48.572				6
	MOTA	1016		A 128	49.779				6
	MOTA	1017		A 128	49.505				
	MOTA	1018		A 128	48.855				
	MOTA	1019			48.625 50.792				
55		1020		A 128 A 128	51.98				8
	MOTA	1021		A 128 A 129	50.32				7
	MOTA	1022		A 129	51.24			7 1.00 79.65	6
	MOTA	1023 1024		A 129	50.50			5 1.00 79.08	
60	MOTA TOM	1024		A 129	51.42		57.01		
00	MOTA	1026			51.00	0 25.097	7 57.33	8 1.00 80.12	. 8

						-89				
	ATOM	1027	ODS	ASP A	129	52.578	23.546	57.311	1.00 80.59	8
	MOTA	1028	C	ASP A		52.085	21.164	55.676	1.00 80.77	6
	ATOM	1029	ō	ASP A		53.089	21.441	56.355	1.00 80.25	8
	ATOM	1030	N	THR A		51.724	19.907	55.389	1.00 80.58	7
5	ATOM	1031	CA	THR A		52.541	18.824	55.925	1.00 81.44	6
•	ATOM	1032	СВ	THR A		52.508	18.858	57.465	1.00 83.89	· 6
	MOTA	1033	OG1	THR A		51.433	19.722	57.880	1.00 85.49	8
	ATOM	1034	CG2	THR A		53.882	19.331	58.047	1.00 83.12	6
	MOTA	1035	С	THR A		52.309	17.374	55.529	1.00 80.12	6
10	MOTA	1036	0	THR A	130	51.199	16.974	55.148	1.00 78.43	8
	MOTA	1037	N	GLU A	131	53.404	16.611	55.654	1.00 79.90	7
	ATOM	1038	CA	GLU A	131	53.459	15.165	55.432	1.00 80.19	6
	MOTA	1039	СВ	GLU A	131	52.364	14.489	56.272	1.00 82.93	6
	MOTA	1040	CG	GLU A	131	52.693	14.372	57.760	1.00 86.59	6
15	MOTA	1041	CD	GLU A	131	51.440	14.289	58.632	1.00 88.67	6
	MOTA	1042	OE1	GLU A	131	50.524	13.470	58.311	1.00 89.43	8
	MOTA	1043	OE2	GLU A	131	51.380	15.050	59.638	1.00 88.79	8
	MOTA	1044	С	GLU A	131	53.378	14.637	54.012	1.00 79.05	6
	MOTA	1045	0	GLU A		54.337	14.716	53.231	1.00 77.86	8
20	MOTA	1046	N	SER A		52.227	14.033	53.727	1.00 77.68	7
	MOTA	1047	CA	SER A		51.915	13.474	52.426	1.00 76.46	6
	MOTA	1048	CB	SER A		50.796	12.429	52.576	1.00 76.05	6
	MOTA	1049	OG	SER A		49.642	12.990	53.176	1.00 74.46	8
0=	MOTA	1050	С	SER A		51.462	14.653	51.533	1.00 75.70	6
25	MOTA	1051	0	SER A		51.123	14.479	50.355	1.00 75.58	8
	MOTA	1052	N	GLY A		51.468	15.848	52.127	1.00 73.94	7
	MOTA	1053	CA	GLY A		51.094	17.056	51.421	1.00 71.52	6
	MOTA	1054	C	GLY A		49.754	16.971	50.735	1.00 70.11	6 8
20	MOTA	1055	0	GLY A		48.927	16.115	51.060	1.00 69.95 1.00 68.35	7
30	MOTA	1056	N	ALA A		49.540	17.864 17.895	49.774 49.033	1.00 65.73	6
	MOTA	1057	CA	ALA A		48.290 47.748	19.321	48.982	1.00 65.73	6
	MOTA	1058	CB	ALA A		48.476	17.359	47.621	1.00 63.87	6
	MOTA MOTA	1059 1060	C O	ALA A		49.600	17.219	47.124	1.00 61.93	8
35	ATOM	1061	N	THR A		47.353	17.048	46.985	1.00 63.38	7
00	ATOM	1062	CA	THR A		47.359	16.549	45.621	1.00 62.44	6
	ATOM	1063	CB	THR A		47.003	15.066	45.562	1.00 62.52	6
	MOTA	1064		THR A		47.951	14.323	46.345	1.00 62.25	8
	ATOM	1065		THR A		47.040	14.574	44,122	1.00 61.31	6
40	ATOM	1066	C	THR A		46.350	17.355	44.820	1.00 61.68	6
. •	ATOM	1067	ō	THR A		45.120	17.188	44.944	1.00 60.36	8
	MOTA	1068	N	CYS A	136	46.900	18.259	44.017	1.00 59.30	7
	MOTA	1069	CA	CYS A	136	46.115	19.129	43.178	1.00 56.11	6
	MOTA	1070	С	CYS A	136	46.111	18.538	41.778	1.00 55.58	6
45	MOTA	1071	0	CYS A	136	47.168	18.370	41.163	1.00 53.10	8
	MOTA	1072	CB	CYS A	136	46.739	20.518	43.181	1.00 55.44	6
	ATOM	1073	SG	CYS A	136	46.010	21.663	41.978	1.00 54.51	16
	MOTA	1074	N	ARG A		44.917	18.191	41.298	1.00 55.48	7
	MOTA	1075	CA	ARG A		44.764	17.611	39.968	1.00 56.07	6
50	MOTA	1076	CB	ARG A		43.786	16.431	39.990	1.00 58.27	6
	ATOM	1077	CG	ARG A		44.213	15.318	40.915	1.00 62.94	6
	ATOM	1078	CD	ARG A		43.017	14.517	41.384	1.00 67.01	6
	MOTA	1079	NE	ARG A		43.308	13.821	42.641	1.00 72.70	7
EE	MOTA	1080	CZ	ARG A		44.131	12.772	42.762	1.00 74.69 1.00 74.12	6 7
55	MOTA	1081		ARG A		44.765	12.270	41.696 43.958	1.00 74.12	7 7
	MOTA	1082		ARG A		44.326 44.265	12.226 18.670	39.010	1.00 74.27	6
	MOTA	1083 1084	C	ARG A		43.325	19.396	39.301	1.00 51.52	8
	MOTA .	1084	N O	ILE A		44.917	18.738	37.860	1.00 52.05	. 7
60	MOTA	1085	CA	ILE A		44.582	19.696	36.825	1.00 50.25	6
-	MOTA	1087	CB	ILE A		45.778	20.624	36.557	1.00 49.78	6
		_00,		••		30 0	· · ·			_

PCT/EP01/01457

						-90				
	7/0014	1000	000 1	LE A	12Ω	45.449	21.566	35.421	1.00 48.31	6
	MOTA	1088 1089		LLE A		46.150	21.389	37.837	1.00 48.07	6
	ATOM ATOM	1089		ILE A		47.444	22.144	37.750	1.00 41.58	6
	ATOM	1091		ILE A		44.270	18.925	35.555	1.00 49.76	6
5	MOTA	1092	_	LLE A		45.119	18.190	35.058	1.00 50.40	8
•	ATOM	1093	_	LYS A		43.059	19.081	35.032	1.00 49.44	7
	ATOM	1094		LYS A		42.672	18.374	33.809	1.00 51.81	6
	ATOM	1095		LYS A		41.285	17.713	33.969	1.00 52.86	6
	MOTA	1096		LYS A		41.176	16.772	35.164	1.00 56.41	6
10	ATOM	1097		LYS A		39.919	15.940	35.137	1.00 57.01	6
	ATOM	1098	CE I	LYS A	139	39.978	14.888	34.047	1.00 60.31	6
	MOTA	1099		LYS A		38.728	14.066	33.965	1.00 59.02	7
	MOTA	1100		LYS A		42.628	19.317	32.615	1.00 51.20	6
	MOTA	1101		LYS A		41.964	20.340	32.673	1.00 51.87	8
15	MOTA	1102		ILE A		43.325	18.979	31.535	1.00 49.23	7
	MOTA	1103		ILE A		43.295	19.826	30.354	1.00 49.38 1.00 50.36	6 6
	MOTA	1104		ILE A		44.578	20.710	30.278	1.00 50.36	6
	MOTA	1105		ILE A		44.889	21.277	31.653 29.868	1.00 51.45	6
00	MOTA	1106		ILE A		45.794 47.103	19.900 20.630	30.148	1.00 50.02	6
20	ATOM	1107	_	ILE A		43.088	19.025	29.066	1.00 47.91	6
	MOTA	1108		ILE A		43.721	18.006	28.859	1.00 46.67	8
	MOTA MOTA	1109 1110	-	GLY A		42.168	19.485	28.220	1.00 48.53	7
	MOTA	1111		GLY A		41.885	18.811	26.959	1.00 47.60	6
25	ATOM	1112		GLY A		41.255	19.765	25.958	1.00 48.49	6
_0	ATOM	1113		GLY A		40.938	20.900	26.317	1.00 49.03	8
	ATOM	1114		SER A		41.070	19.329	24.712	1.00 46.01	7
	ATOM	1115		SER A		40.466	20.195	23.699	1.00 43.95	6
	MOTA	1116		SER A		40.306	19.466	22.370	1.00 44.36	6
30	ATOM	1117	OG	SER A	142	39.494	20.214	21.477	1.00 39.73	8
	ATOM	1118	С	SER A	142	39.107	20.686	24.144	1.00 45.09	6
	MOTA	1119	0	SER A	142	38.319	19.934	24.714	1.00 47.13	8
	MOTA	1120	N	TRP A	143	38.822	21.947	23.862	1.00 43.97	7
	MOTA	1121		TRP A		37.564	22,537	24.256	1.00 41.28	6
35	MOTA	1122		TRP A		37.754	24.033	24.473	1.00 42.28	6 6
	MOTA	1123	CG	TRP A		36.577	24.697	25.126	1.00 42.52 1.00 39.43	6
	MOTA	1124		TRP A		36.215	24.610	26.505 26.676	1.00 39.43	6
	MOTA	1125		TRP A		35.025	25.359 23.969	27.613	1.00 37.16	6
40	MOTA	1126		TRP A		36.778 35.618	25.480	24.526	1.00 37.10	6
40	MOTA	1127		TRP A		34.681	25.880	25.456	1.00 40.50	7
	MOTA	1128 1129		TRP A		34.393	25.480	27.911	1.00 39.06	6
	MOTA MOTA	1130	CZ3	TRP A		36.150	24.090	28.837	1.00 39.37	6
	MOTA	1131		TRP A		34.968	24.840	28.978	1.00 39.40	6
45	MOTA	1132		TRP A	•	36,450		23.258	1.00 41.37	6
	MOTA	1133	ō	TRP A		35.287	22.239	23.632	1.00 42.45	8
	MOTA	1134	N	THR A		36.790	22.179	21.983	1.00 41.97	7
	MOTA	1135	CA	THR A		35.760	21.992	20.979	1.00 41.13	6
	MOTA	1136	CB	THR A		35.703	23.191	20.051	1.00 39.00	6
50	MOTA	1137	OG1	THR A	144	36.994	23.416	19.490	1.00 39.19	8
	MOTA	1138	CG2	THR A		35.288	24.420	20.818	1.00 37.78	6
	MOTA	1139	C	THR A		35.879	20,738	20.148	1.00 42.54	6
	MOTA	1140	0	THR A		34.941	20.385	19.443	1.00 45.82	8
	MOTA	1141		HIS A		37.012	20.054	20.233	1.00 43.18 1.00 46.20	7
55	MOTA	1142		HIS A		37.187	18.837	19.459		6 6
	MOTA	1143		HIS A		38.517	18.875	18.707	1.00 46.05	6
	MOTA	1144		HIS A		38.588	19.933	17.646	1.00 46.56 1.00 45.44	6 6
	MOTA	1145		HIS A		37.994	20.022	16.432 17.772	1.00 45.44	7
60	MOTA	1146	ND1	HIS A	145	39.366 39.250	21.061 21.797	16.682	1.00 43.87	6
60	MOTA	1147		HIS A		38.423	21.737	15.853	1.00 41.35	7
	MOTA	1148	MES	LITO F	* ***	50.425	22.200			•

						0.1					
						-91	12 520	20 202	1 00	17 26	6
	MOTA	1149		HIS A		37.105	17.570	20.303	1.00		8
	MOTA	1150		HIS A		37.811	17.422	21.298 19.898	1.00		7
	ATOM	1151		HIS A		36.230	16.656 15.400	20.609	1.00		6
_	ATOM	1152		HIS A		36.067	14.846	20.365	1.00		6
5	MOTA	1153		HIS A		34.658	14.694	18.919	1.00		· 6
	ATOM	1154	CG	HIS A		34.314	14.057	17.910		50.68	6
	ATOM	1155		HIS A		34.954	15.248	18.362	1.00		7
	MOTA	1156		HIS A	_	33.183 33.138	14.962	17.073		49.57	6
10	MOTA	1157		HIS A		34.202	14.239	16.774		51.03	7
10	MOTA	1158		HIS A		37.137	14.396	20.167		49.74	6
	MOTA	1159	C	HIS A		37.137	14.673	19.268		49.87	8
	MOTA	1160		HIS A		37.145	13.234	20.809		50.23	7
	MOTA	1161	N	SER A		38.101	12.158	20.543		50.98	6
4 =	MOTA	1162	CA	SER A		37.722	10.934	21.372		50.73	6
15	MOTA	1163	CB OG	SER A		36.346	10.642	21.240		51.84	8
	MOTA	1164	C	SER A		38.314	11.730	19.096		51.53	6
	MOTA	1165 1166		SER A		39.374	11.228	18.754		50.53	8
	MOTA	1167	N O	ARG A		37.319	11.925	18.245		53.75	7
20	MOTA	1168	CA	ARG A		37.444	11.528	16.850		56.68	6
20	MOTA MOTA	1169	CB	ARG A		36.052	11.408	16.221		60.77	6
	ATOM	1170	CG	ARG A		35.100	10.487	16.985		70.28	6
	ATOM	1171	CD	ARG A		33.673	10.516	16.423		76.18	6
	ATOM	1172	NE	ARG A		32.702	9.919	17.351		83.11	7
25	ATOM	1173	CZ	ARG A		32.685	8.632	17.719	1.00	85.65	6
	ATOM	1174		ARG A		33.595	7.781	17.243	1.00	86.70	7
	ATOM	1175		ARG A		31.746	8.187	18.549	1.00	85.60	7
	MOTA	1176	C	ARG A		38.295	12.502	16.025	1.00	56.73	6
	ATOM	1177	ō	ARG A		38.774	12.157	14.938	1.00	56.48	8
30	MOTA	1178	N	GLU A	149	38.477	13.714	16.553	1.00	55.77	7
	ATOM	1179	CA	GLU A		39.233	14.767	15.884	1.00	51.96	6
	MOTA	1180	CB	GLU A	149	38.384	16.037	15.821	1.00	52.02	6
	ATOM	1181	CG	GLU A	149	36.918	15.748	15.527		51.38	6
	MOTA	1182	CD	GLU A	149	36.065	16.989	15,423		49.98	6
35	MOTA	1183	OE1	GLU A	. 149	36.220	17.879	16.273		50.58	8
	MOTA	1184	OE2	GLU A	149	35.226	17.070	14.506		46.84	8
	MOTA	1185	С	GLU A	. 149	40.531	15.030	16.627		50.15	6
	MOTA	1186	0	GLU A	149	41.584	15.167	16.013		49.33	8
	MOTA	1187	Ν.	ILE A		40.454	15.100	17.950		47.25	7
40	MOTA	1188	CA	ILE A		41.643	15.309	18.748		48.44	6
	MOTA	1189	CB	ILE A		41.712	16.740	19.374		48.83	6
	MOTA	1190	CG2			42.759	16.793	20.481		44.42	6
	MOTA	1191	CG1			42.104	17.769	18.316		49.22	6
	ATOM	1192		ILE F		42.185	19.175	18.839		45.68	6 6
45	MOTA	1193	_			41.707		19.881		50.37 50.37	8
	ATOM	1194	0	ILE A	120	40.712	14.031	20.536 20.104		52.48	7
	MOTA	1195	N	SER A		42.902	13.781	21.178		54.49	6
	MOTA	1196	CA	SER A		43.156	12.841 11.452	20.611		54.22	6
EΩ	MOTA	1197	CB	SER A		43.437 44.619	11.452	19.844		54.28	8
50	MOTA	1198	OG	SER A		44.385	13.381	21.899		55.57	6
	MOTA	1199	C	SER A	1 151	45.347	13.798	21.257		56.29	8
	MOTA	1200	0	VAL A		44.337	13.400	23.227		57.03	7
	MOTA	1201 1202	N CA	VAL A		45.447	13.400	24.033		59.85	6
55	MOTA	1202	CB	VAL Z		44.979	14.922	25.100		59.80	6
J	ATOM ATOM	1203		VAL A		44.170	16.021	24.447		60.14	6
	MOTA	1204		VAL 2		44.163	14.225	26.175		61.09	6
	ATOM	1205	C	VAL		46.084	12.722	24.747		61.00	6
	ATOM	1207	0	VAL		45.393	11.785	25.132		59.83	8
60	ATOM	1208	N		A 153	47.398	12.780	24.932		63.57	7
	MOTA	1209	CA		A 153	48.114	11.690	25.582	1.00	66.72	6

					-92				
	MOTA	1210	CB Z	ASP A 153	48.620	10.724	24.505	1.00 66.16	6
	ATOM	1211		ASP A 153	47.505	10.245	23.573	1.00 67.72	6
	ATOM	1212		ASP A 153	46.769	9.317	23.972	1.00 68.96	8
	ATOM	1213		ASP A 153	47.354	10.801	22.451	1.00 67.60	8
5	MOTA	1214	C Z	ASP A 153	49.293	12.198	26.422	1.00 68.93	6
	MOTA	1215	0 2	ASP A 153	49.951	13.175	26.058	1.00 69.39	8
	MOTA	1216	N	PRO A 154	49.553	11.564	27.577	1.00 70.74	7
	MOTA	1217		PRO A 154	48.601	10.759	28.357	1.00 71.40	6 6
	MOTA	1218		PRO A 154	50.675	11.995	28.421	1.00 73.42 1.00 72.22	6
10	MOTA	1219		PRO A 154	50.421	11.266	29.735 29.776	1.00 72.22	6
	ATOM	1220		PRO A 154	48.930	11.182 11.580	27.773	1.00 72.37	6
	MOTA	1221		PRO A 154	51.999 51.997	10.951	26.716	1.00 75.49	8
	MOTA	1222	_	PRO A 154	53.121	11.916	28.406	1.00 79.97	7
4 =	ATOM	1223		THR A 155 THR A 155	54.433	11.580	27.851	1.00 84.54	6
15	MOTA	1224		THR A 155	55.002	12.797	27.084	1.00 84.38	6
	MOTA	1225 1226		THR A 155	55.314	13.844	28.015	1.00 85.24	8
	MOTA MOTA	1227		THR A 155	53.979	13.326	26.085	1.00 83.86	6
	MOTA	1228		THR A 155	55.504	11.101	28.868	1.00.88.31	6
20	ATOM	1229		THR A 155	55.179	10.480	29.905	1.00 89.23	8
20	ATOM	1230	N	THR A 156	56.774	11.402	28.539	1.00 91.22	7
	ATOM	1231		THR A 156	57.970	11.057	29.337	1.00 93.64	6
	MOTA	1232	CB	THR A 156	59.146	12.041	29.041	1.00 93.80	6
	ATOM	1233		THR A 156	59.430	12.048	27.631	1.00 93.55	8
25	MOTA	1234		THR A 156	60.414	11.624	29.839	1.00 93.12	6
	MOTA	1235	С	THR A 156	57.778	11.031	30.862	1.00 95.49	6
	MOTA	1236	0	THR A 156	57.812	12.080	31.532	1.00 95.50	8
	MOTA	1237	N	GLU A 157	57.614	9.827	31.406	1.00 97.12	7
	MOTA	1238	CA	GLU A 157	57.411	9.649	32.841	1.00 98.24	6
30	MOTA	1239	CB	GLU A 157	56.619	8.370	33.095	1.00100.23	6 6
	MOTA	1240	CG	GLU A 157	55.476	8.150	32.109	1.00103.23	
	MOTA	1241	CD	GLU A 157	54.728	6.842	32.372	1.00104.38 1.00103.49	6 8
	MOTA	1242		GLU A 157	55.391	5.769	32.462 32.482	1.00105.49	8
0.5	MOTA	1243		GLU A 157	53.475	6.896 9.570	33.591	1.00103.11	6
35	MOTA	1244	C	GLU A 157	58.731 58.742	9.488	34.825	1.00 98.77	8
	MOTA	1245	0	GLU A 157 ASN A 158	59.840	9.582	32.854	1.00 97.95	7
	MOTA	1246	N	ASN A 158	61.154	9.505	33.494	1.00 98.34	6
	MOTA	1247	CA CB	ASN A 158	62.244	9.212	32.455	1.00100.52	6
40	MOTA MOTA	1248 1249	CG	ASN A 158	61.953	7.969	31.634	1.00102.32	6
40	ATOM	1250		ASN A 158	61.787	6.872	32.184	1.00104.16	8
	ATOM	1251		ASN A 158	61.898	8.131	30.305	1.00102.61	7
	MOTA	1252	C	ASN A 158	61.471	10.832	34.196	1.00 97.02	6
	MOTA	1253	ō	ASN A 158	61.170	11.019	35.392	1.00 96.34	8
45	ATOM	1254	N	SER A 159	62.093	11.729	33.423	1.00 94.95	7
	ATOM	1255	CA	SER A 159	62.492	13.069	33.857	1.00 91.51	6
	MOTA	1256	CB	SER A 159	61.878	14.091	32.890	1.00 91.99	6
	MOTA	1257	OG	SER A 159	60.550	13.708	32.529	1.00 90.83	8
	MOTA	1258	С	SER A 159	62.116	13.412	35.301	1.00 88.77	6
50	MOTA	1259		SER A 159	60.939	13.380	35.666	1.00 88.38 1.00 85.60	8 7
	MOTA	1260		ASP A 160	63.120	13.728	36.120	1.00 83.60	6
	MOTA	1261		ASP A 160	62.867	14.093	37.517	1.00 81.09	6
	MOTA	1262		ASP A 160	64.107	14.716 15.217	38.164 39.578	1.00 81.79	6
	MOTA	1263	CG	ASP A 160	63.827 64.609		40.075	1.00 82.10	8
55	MOTA	1264		ASP A 160	62.824		40.073	1.00 81.33	8
	MOTA	1265		ASP A 160 ASP A 160	61.748		37.556	1.00 78.87	6
	MOTA	1266		ASP A 160	61.906		36.997	1.00 77.29	8
	MOTA	1267 1268		ASP A 160 ASP A 161	60.643		38,223	1.00 75.12	7
60	MOTA MOTA	1269		ASP A 161	59.493		38.324	1.00 71.64	6
00	MOTA	1270		ASP A 161	58.433		39.273	1.00 71.12	6
	A1OM	12/							

						-93				
	MOTA	1271	CG	ASP A	161	57.719	13.895	38.698	1.00 71.43	6
	MOTA	1272		ASP A		57.509	13.854	37.463	1.00 70.50	8
	ATOM	1273		ASP A		57.353	12.983	39.480	1.00 71.76	8
	ATOM	1274	C	ASP A		59.814	17.097	38.756	1.00 69.97	6
5	ATOM	1275	ō	ASP A		59.009	18.001	38.545	1.00 69.41	8
•	MOTA	1276	N	SER A		60.974	17.321	39.358	1.00 68.43	7
	ATOM	1277	CA	SER A		61.282	18.682	39.774	1.00 68.46	6
	ATOM	1278	CB	SER A		61.190	18.809	41.308	1.00 68.76	6
	ATOM	1279	OG	SER A		62.209	18.069	41.962	1.00 68.11	8
10	ATOM	1280	c	SER A		62.636	19.163	39.289	1.00 67.78	6
. •	MOTA	1281	ō	SER A		63.264	20.014	39.917	1.00 67.84	8
	MOTA	1282	N	GLU A		63.087	18.640	38.156	1.00 67.60	7
	MOTA	1283	CA	GLU A		64.382	19.052	37.649	1.00 68.35	6
	ATOM	1284	CB	GLU A	163	64.884	18.051	36.609	1.00 70.48	6
15	MOTA	1285	CG	GLU A		64.380	18.242	35.193	1.00 73.24	. 6
	ATOM	1286	CD	GLU A		65.111	17.328	34.204	1.00 75.50	6
	MOTA	1287	OE1	GLU A		64.835	16.097	34.211	1.00 76.99	8
	MOTA	1288	OE2	GLU A		65.970	17.842	33.438	1.00 73.24	8
	MOTA	1289	С	GLU A		64.342	20.475	37.083	1.00 68.50	6
20	MOTA	1290	0	GLU A	163	65.385	21.062	36.774	1.00 69.25	8
	MOTA	1291	N	TYR A	164	63.140	21.031	36.958	1.00 67.44	7
	ATOM	1292	CA	TYR A	164	62.968	22.396	36.466	1.00 65.48	6
	MOTA	1293	CB	TYR A	164	62.085	22.422	35.221	1.00 66.46	6
	MOTA	1294	CG	TYR A	164	62.709	21.754	34.029	1.00 67.56	6
25	MOTA	1295	CD1	TYR A	164	62.082	20.664	33.415	1.00 68.14	6
	MOTA	1296	CE1	TYR A	164	62.664	20.011	32.328	1.00 67.68	6
	ATOM	1297	CD2	TYR A	164	63.942	22.185	33.527	1.00 66.99	6
	ATOM	1298	CE2	TYR A	164	64.539	21.538	32.435	1.00 69.28	6
	MOTA	1299	cz	TYR A	164	63.892	20.449	31.837	1.00 68.44	6
30	ATOM	1300	OH	TYR A	164	64.456	19.823	30.737	1.00 69.00	8
	ATOM	1301	С	TYR A	164	62.313	23.259	37.534	1.00 64.21	6
	MOTA	1302	0	TYR A	164	62.181	24.474	37.368	1.00 62.71	8
	MOTA	1303	N	PHE A	165	61.899	22.626	38.627	1.00 62.72	7
	MOTA	1304	CA	PHE A	165	61.241	23.343	39.705	1.00 60.48	6
35	MOTA	1305	CB	PHE A	165	60.738	22.364	40.758	1.00 57.99	6
	MOTA	1306	CG	PHE A		59.676	22.936	41.641	1.00 57.14	6
	MOTA	1307	CD1	PHE A	165	58.424	23.252	41.115	1.00 55.84	6
	MOTA	1308		PHE A		59.933	23.194	42.985	1.00 55.03	6
	MOTA	1309		PHE A		57.439	23.818	41.902	1.00 54.80	6
40	MOTA	1310		PHE A		58.961	23.762	43.787	1.00 57.75	6
	MOTA	1311	CZ	PHE A		57.699	24.079	43.242	1.00 57.78	6
	MOTA	1312	С	PHE A		62.159	24.369	40.354	1.00 60.44	6
	MOTA	1313	0	PHE A		63.348	24.121	40.547	1.00 60.73	8
4 =	MOTA	1314	N	SER A		61.611	25.534	40.676	1.00 60.95	7
45	ATOM	1315	CA	SER A		62.418	26.567	41.312	1.00 61.11	6
	ATOM	1316		SER A		61.638		41.457		6
	ATOM	1317	OG	SER A		62.476	28.875	42.015	1.00 59.79 1.00 61.38	8
	ATOM	1318	C	SER A		62.809	26.068	42.694	_	6
EΩ	ATOM	1319	0	SER A		62.009	25.442	43.393	1.00 61.62 1.00 61.82	8
50	ATOM	1320	N	GLN A		64.038	26.359	43.089	1.00 61.82	7
	MOTA	1321	CA	GLN A		64.525	25.931	44.393	1.00 62.17	6 6
	MOTA	1322	CB	GLN A		66.052	25.797	44.351	1.00 65.38	
	MOTA	1323	CG	GLN A		66.745 68.204	27.065 26.851	43.861 43.514	1.00 69.06	6 6
55	MOTA	1324	CD OF1	GLN A		69.008	26.851	43.314	1.00 69.06	8
J	ATOM ATOM	1325 1326	NE2	GLN A		68.556	27.081	42.241	1.00 70.77	7
	ATOM	1326		GLN A		64.119	26.927	45.476	1.00 61.23	6
	ATOM	1328	C O	GLN A		64.112	26.585	46.659	1.00 61.22	8
	ATOM	1329	Ŋ	TYR A		63.762	28.147	45.075	1.00 58.44	7
60	MOTA	1330	CA	TYR A		63.702	29.162	46.046	1.00 56.45	6
55	MOTA	1331	CB	TYR A		63.881	30.522	45.564	1.00 55.36	6
	0	±331				55.551				-

						-94					
	ATOM	1332	CG	TYR A 1	L68	65.335	30.469	45.158	1.00 5	57.58	6
	ATOM	1333		TYR A		65.699	30.352	43.818	1.00 !	57.60	6
	ATOM	1334	_	TYR A	_	67.031	30.233	43.439	1.00 !	57.86	6
	ATOM	1335		TYR A		66.349	30.467	46.115	1.00		6
5	ATOM	1336	CE2	TYR A	168	67.683	30.347	45.749	1.00		6
_	ATOM	1337	CZ	TYR A	168	68.017	30.228	44.410	1.00		. 6
	ATOM	1338	OH	TYR A	168	69.337	30.086	44.042	1.00		8
	MOTA	1339	С	TYR A	168	61.912	29.199	46.383	1.00		6
	MOTA	1340	0	TYR A	168	61.457	30.053	47.142	1.00		8
10	MOTA	1341	N	SER A	169	61.162	28.257	45.832	1.00		7
	MOTA	1342	CA	SER A		59.732	28.179	46.096	1.00		6
	ATOM	1343	CB	SER A	169	59.082	27.123	45.197	1.00		6
	MOTA	1344	OG	SER A	169	57.699	26.971	45.501	1.00		8
	ATOM	1345	С	SER A		59.478	27.804	47.544	1.00		6
15	MOTA	1346	0	SER A	169	60.246	27.066	48.152		58.82	8
	MOTA	1347	N	ARG A		58.385	28.302	48.096		58.68	7
	MOTA	1348	CA	ARG A	170	58.043	27.993	49.472		58.62	6
	MOTA	1349	CB	ARG A		56.907	28.901	49.956		60.14	6
	MOTA	1350	CG	ARG A		57.371	30.123	50.727		60.43	6 6
20	MOTA	1351	CD	ARG A		56.401	31.291	50.589		64.30	7
	MOTA	1352	NE	ARG A		55.020	30.998	50.989		66.31	6
	MOTA	1353	CZ	ARG A		53.967	31.107	50.174 48.915		66.81 63.97	7
	MOTA	1354		ARG A		54.129	31.489	50.619		67.23	7
0.5	MOTA	1355	NH2			52.750	30.850 26.544	49.554		58.75	6
25	MOTA	1356	C	ARG A		57.604		50.642		60.59	8
	MOTA	1357	0	ARG A		57.516	25.975 25.933	48.405		57.02	7
	MOTA	1358	N	PHE A		57.339	24.552	48.404		56.54	6
	MOTA	1359	CA	PHE A		56.882 55.499	24.332	47.765		55.41	6
20	ATOM	1360	CB	PHE A		54.552	25.522	48.281		55.91	6
30	MOTA	1361	CG	PHE A		54.685	26.856	47.893		57.70	6
	MOTA	1362		PHE A		53.560	25.190	49.203		56.28	6
	MOTA	1363 1364		PHE A		53.845	27.847	48.419		58.19	6
	MOTA MOTA	1365		PHE A		52.718	26.170	49.732		55.91	6
35	MOTA	1366	CZ	PHE A		52.864	27.505	49.337	1.00	57.16	6
00	ATOM	1367	C	PHE A		57.844	23.612	47.695	1.00	56.77	6
	ATOM	1368	Ö	PHE A		58.841	24.045	47.113	1.00	56.03	8
	ATOM	1369	N	GLU A		57.552	22.319	47.765	1.00	56.23	7
	ATOM	1370	CA	GLU A		58.389	21.325	47.120	1.00	58.00	6
40	ATOM	1371	СВ	GLU A		59.371	20.707	48.119		60.23	6
	ATOM	1372	CG	GLU A	172	58.734	19.970	49.303	1.00	64.00	6
	MOTA	1373	CD	GLU A	172	59.769	19.445	50.313		66.01	6
	MOTA	1374	OE1	. GLU A	172	60.869	19.042	49.868		69.59	8
	MOTA	1375	OE2	GLU A	172	59.487	19.421	51.541		65.33	8
45	MOTA	1376	C	GLU A		57.497	20.259	46.518		59.67	6
	ATOM	1377	0	GLU A	172	56.356		46.955		60.12	8
	MOTA	1378	N	ILE A		58.006	19.579	45.496		60.16	7
	MOTA	1379	CA	ILE A				44.827		60.67	6
	MOTA	1380	СВ	ILE A		57.413	18.587	43.291		61.87	6 6
50	MOTA	1381		2 ILE A		56.659		42.644		62.56 61.03	6
	MOTA	1382		L ILE A		56.920		42.727		59.49	6
	MOTA	1383		L ILE A		57.165		41.244 45.296		59.83	6
	MOTA	1384		ILE A		57.579		45.290		57.21	8
	MOTA	1385	0	ILE A		58.751		45.616		61.63	7
55	MOTA	1386		LEU A		56.554 56.786		46.056		64.20	6
	MOTA	1387		LEU A		56.786 55.687		47.024		63.47	6
	MOTA	1388		LEU A LEU A		55.461		48.149		65.34	6
	MOTA	1389	CG	LEU A 1 LEU A		54.285		49.024		66.19	6
60	MOTA MOTA	1390 1391		LEU A		56.747		48.962		64.00	6
50	ATOM	1392		LEU A		56.783		44.806		65.92	6
	ATOH	1372	_		-·-						

PCT/EP01/01457

						-95						
	2001	1202	^ ,	LEU A	174	57.75	57	13.440	44.522	1.00 6	55.29	8
	MOTA	1393 1394		ASP A		55.70		14.233	44.036	1.00 6		7
	MOTA	1394		ASP A		55.58		13.436	42.827	1.00 6	8.45	6
	MOTA	1396		ASP A		55.23		11.993	43.223	1.00 6		6
5	ATOM ATOM	1397		ASP A		55.1		11.038	42.032	1.00	58.23	6
5		1398		ASP A		56.1		10.964	41.244	1.00	67.58	8
	MOTA	1399		ASP A		54.1		10.347	41.905	1.00	67.56	8
	MOTA	1400	C	ASP A	175	54.5		14.023	41.872	1.00		6
	MOTA MOTA	1401		ASP A		53.6		14.735	42.286	1.00		8
10	ATOM	1402		VAL A		54.7		13.727	40.587	1.00		7
10	ATOM	1403		VAL A		53.8		14.198	39.552	1.00	67.76	6
	ATOM	1404		VAL A		54.4		15.324	38.694	1.00	67.60	6
	MOTA	1405		VAL A		53.5		15.721	37.542	1.00	66.09	6
	ATOM	1406		VAL A		54.7	71	16.532	39.564	1.00	65.31	6
15	ATOM	1407		VAL A		53.4		13.025	38.645	1.00		6
••	ATOM	1408		VAL A		54.3	99	12.308	38.230	1.00	66.10	8
	ATOM	1409	N	THR A		52.2	13	12.833	38.348		68.30	7
	MOTA	1410	CA	THR A		51.7	81	11.763	37.463	1.00	69.37	6
	MOTA	1411	СВ	THR A		51.2	41	10.565	38.259		69.49	6
20	ATOM	1412		THR A		50.2	18	11.007	39.160		69.60	8
20	MOTA	1413	CG2	THR A		52.3	66	9.905	39.045		69.19	6
	ATOM	1414	C	THR A		50.6	96	12.276	36.528		70.72	6
	ATOM	1415	ō	THR A		49.8	79	13.119	36.917		72.04	8
	ATOM	1416	Ŋ	GLN A	178	50.€	92	11.771	35.297		71.85	7
25	ATOM	1417	CA	GLN A		49.7	06	12.191	34.302	1.00	73.03	6
	MOTA	1418	СВ	GLN A		50.3	92	12.916	33.144		75.20	6
	ATOM	1419	CG	GLN A	178	51.€	81	13.640	33.533		78.41	6
	MOTA	1420	CD	GLN A	178	52.0)59	14.733	32.539		79.92	6
	ATOM	1421	OE1	GLN A		52.0	78	14.509	31.315		81.52	8
30	ATOM	1422	NE2	GLN A	178	52.3	370	15.924	33.061		78.36	7
	ATOM	1423	С	GLN F		49.0		10.964	33.764		72.67	6
	MOTA	1424	0	GLN F		49.6		10.043	33.293		73.74	8
	ATOM	1425	N	LYS A		47.6		10.947	33.827		72.17	7
	MOTA	1426	CA	LYS ?		46.9		9.807	33.337		71.53	6 6
35	MOTA	1427	CB	LYS A		46.3		9.038	34.519		74.09	6
	ATOM	1428	CG	LYS 2		47.		8.781	35.644		79.46	6
	MOTA	1429	CD	LYS A		46.		8.189	36.905		81.06	6
	MOTA	1430	CE		A 179	47.		8.300	38.119		80.77 80.83	7
	MOTA	1431	NZ		A 179	47.		9.715	38.443		70.00	6
40	MOTA	1432	С		A 179	45.		10.316	32.470		73.37	8
	MOTA	1433	0		A 179	44.		10.939	32.980 31.170		67.55	7
	MOTA	1434	N		A 180	45.		10.060	30.294		67.72	6
	MOTA	1435	CA		A 180	44.		10.538 10.327	28.829		66.54	6
	MOTA	1436	CB		A 180	45.		8.909	28.344		63.87	6
45	ATOM	1437		LYS .		45.	751	8.573	27.796		64.72	6
	ATOM	1438	CD		A 180		404	9.412	26.552		65.43	6
	MOTA	1439	CE		A 180		217	9.057	25.339		65.01	7
	ATOM	1440	NZ		A 180		445	9.854	30.586		67.22	6
	MOTA	1441	C	PAR	A 180 A 180		373	9.021	31.471		68.12	8
50	ATOM	1442			A 181		388	10.231	29.871		67.59	7
	MOTA	1443			A 181		083	9.600	30.053		68.03	6
	MOTA	1444			A 181		710	9.514	31.545	1.00	69.44	6
	MOTA	1445 1446			A 181		940	10.803	32.291		68.81	6
55	ATOM ATOM	1440			A 181		552	11.872	31.834		71.29	8
55	ATOM	1447	בעות :	2 ASN	A 181		556	10.706	33.463	1.00	67.88	7
	MOTA	1449			A 181		917	10.194			67.66	· 6
	ATOM	1450		ASN	A 181		576	11.350	29.437		68.16	8
	MOTA	1451			A 182		302	9.377	28.420		68.81	7
60	MOTA	1452			A 182		160	9.802	27.615		68.00	6
	ATOM	1453			A 182	37	861	8.745	26.553	1.00	67.42	6

					-96				
	MOTA	1454	OG	SER A 182	36.905	9.223	25.626	1.00 70.87	8
	ATOM	1455	C	SER A 182	36.953	9.974	28.541	1.00 67.36	6
	MOTA	1456	0	SER A 182	36.915	9.385	29.617	1.00 67.61	8
	MOTA	1457	N	VAL A 183	35.973	10.771	28.126	1.00 65.82	7
5	MOTA	1458	CA	VAL A 183	34.790	11.017	28.950	1.00 64.66	. 6
•	MOTA	1459	CB	VAL A 183	35.151	11.912	30.163	1.00 63.68	· 6
	MOTA	1460		VAL A 183	36.153	12.956	29.748	1.00 65.08	6 6
	MOTA	1461		VAL A 183	33.901	12.581	30.718	1.00 61.80	6
40	MOTA	1462	C	VAL A 183	33.632	11.666	28.204	1.00 64.12 1.00 64.83	8
10	MOTA	1463	0	VAL A 183	33.828	12.597	27.440 28.432	1.00 65.00	7
	MOTA	1464	N	THR A 184	32.422 31.240	11.170 11.737	27.793	1.00 67.07	6
	MOTA	1465	CA	THR A 184 THR A 184	30.303	10.641	27.753	1.00 64.63	6
	MOTA	1466	CB	THR A 184	30.977	9.911	26.224	1.00 61.46	8
15	MOTA	1467	CG2		29.030	11.260	26.685	1.00 67.30	6
15	MOTA	1468 1469	CG2	THR A 184	30.490	12.596	28.808	1.00 69.96	6
	ATOM ATOM	1470	0	THR A 184	30.413	12.238	29.993	1.00 71.87	8
	ATOM	1471	N	TYR A 185	29.961	13.735	28.362	1.00.71.00	7
	ATOM	1472	CA	TYR A 185	29.230	14.618	29.261	1.00 72.17	6
· 20	ATOM	1473	CB	TYR A 185	29.849	16.015	29.274	1.00 72.39	б
	ATOM	1474	CG	TYR A 185	31.335	16.005	29.525	1.00 72.53	6
	ATOM	1475		TYR A 185	32.226	15.598	28.531	1.00 71.50	6
	ATOM	1476	CE1	TYR A 185	33.601	15.535	28.775	1.00 70.43	6
	ATOM	1477	CD2	TYR A 185	31.854	16.358	30.776	1.00 73.42	6
25	ATOM	1478	CE2	TYR A 185	33.236	16.300	31.031	1.00 71.16	6
	MOTA	1479	CZ	TYR A 185	34.097	15.885	30.022	1.00 70.35	6
	MOTA	1480	OH	TYR A 185	35.448	15.811	30.254	1.00 68.69	8
	MOTA	1481	С	TYR A 185	27.804	14.705	28.780	1.00 73.84	6
	MOTA	1482	0	TYR A 185	27.551	14.756	27.576	1.00 73.39	8 7
30	MOTA	1483	N	SER A 186	26.873	14.714	29.727	1.00 76.31	6
	MOTA	1484	CA	SER A 186	25.455	14.794	29.403	1.00 78.23 1.00 78.92	6
	MOTA	1485	CB	SER A 186	24.645	14.953	30.693	1.00 73.32	8
	MOTA	1486	OG	SER A 186	25.215	15.952 15.967	31.527 28.453	1.00 77.73	6
0.5	ATOM	1487	C	SER A 186	25.197 24.348	15.879	27.553	1.00 70.25	8
35	MOTA	1488	0	SER A 186	25.949	17.047	28.653	1.00 77.81	7
	MOTA	1489	N	CYS A 187 CYS A 187	25.830	18.254	27.839	1.00 78.71	6
	MOTA	1490 1491	CA C	CYS A 187	26.144	17.978	26.407	1.00 78.06	6
	ATOM ATOM	1492	0	CYS A 187	25.514	18.482	25.488	1.00 78.32	8
40	ATOM	1493	СВ	CYS A 187	,26.858	19.320	28.252	1.00 79.52	6
40	ATOM	1494	SG	CYS A 187	28.656	18.934	27.946	1.00 82.56	16
	ATOM	1495	N	CYS A 188	27.147	17.144	26.244	1.00.78.96	7
	MOTA	1496	CA	CYS A 188	27.706	16.918	24.947	1.00 78.72	6
	ATOM	1497	С	CYS A 188	27.817	15.468	24.454	1.00 78.19	6
45	ATOM	1498	0	CYS A 188	28.454	14.618	25.096	1.00 78.27	8
	ATOM	1499	CB	CYS A 188	29.070	17.610	25.006	1.00 79.96	6
	MOTA	1500	SG	CYS A 188	29.118	19.206	25.950	1.00 80.88	16
	MOTA	1501	N	PRO A 189	27.211	15.186	23.281	1.00 77.44	7
	MOTA	1502	CD	PRO A 189	26.571	16.283	22.526	1.00 77.01	6
50	MOTA	1503	CA	PRO A 189	27.125	13.918	22.532	1.00 76.01 1.00 76.94	6
	MOTA	1504	CB	PRO A 189	26.756	14.378	21.129		6
	MOTA	1505	CG	PRO A 189	25.858	15.558	21.408	1.00 77.54 1.00 75.22	6 6
	MOTA	1506	C	PRO A 189	28.355	12.991 11.883	22.512 23.056	1.00 76.90	8
CE	MOTA	1507	0	PRO A 189	28.300 29.447	13.423	21.874	1.00 70.30	7
55	MOTA	1508	N	GLU A 190 GLU A 190	30.662	12.603	21.768	1.00 69.68	6
	MOTA	1509		GLU A 190	31.535	13.102		1.00 72.91	6
	MOTA	1510 1511		GLU A 190	30.777	13.743	19.486	1.00 75.89	6
	MOTA MOTA	1511 1512			30.236			1.00 77.90	6
60	MOTA	1512		1 GLU A 190	30.974			1.00 78.51	8
55	MOTA	1514		2 GLU A 190	29.080			1.00 79.55	8

						-97				
	MOM	1515		GLU A	100	-97 31.492	12.631	23.039	1.00 66.30	6
	MOTA	1515 1516		GLU A		31.113		24.009	1.00 65.23	8
	MOTA MOTA	1517		ALA A		32.633		23.020	1.00 63.17	7
	MOTA	1517		ALA A		33.524		24.182	1.00 61.94	6
5	ATOM	1519	_	ALA A		34.102		24.341	1.00 60.63	6
5	ATOM	1520		ALA A		34.666		24.055	1.00 61.30	6
	ATOM	1521		ALA A		35.148		22.950	1.00 62.21	8
	ATOM	1522		TYR A		35.105		25.179	1.00 58.30	7
	ATOM	1523		TYR A		36.188		25.159	1.00 56.19	6
10	ATOM	1524		TYR A		35.695		25.633	1.00 55.84	6
	ATOM	1525		TYR A		34.779		24.649	1.00 56.15	6
	ATOM	1526	_	TYR A		33.409		24.642	1.00 56.04	6
	ATOM	1527		TYR A		32.571	16.794	23.683	1.00 57.88	6
	MOTA	1528		TYR A		35.291	17.341	23.675	1.00 56.39	6
15	ATOM	1529		TYR A	192	34.46	17.915	22.715	1.00 57.19	6
	ATOM	1530	CZ	TYR A	192	33.108	17.637	22.722	1.00 58.29	6
	ATOM	1531	OH	TYR A	192	32.29	18.200	21.769	1.00 58.06	8
	ATOM	1532	С	TYR A	192	37.389	14.013	25.984	1.00 56.62	6
	ATOM	1533	0	TYR A		37.37	14.090	27.217	1.00 57.67	8
20	MOTA	1534	N	GLU A	193	38.430	13.571	25.291	1.00 57.15	7
	MOTA	1535	CA	GLU A		39.67	13.124	25.935	1.00 58.07	6
	MOTA	1536	CB	GLU A	193	40.65	12.523	24.901	1.00 56.63	6
	MOTA	1537	CG	GLU A	193	40.14		24.209	1.00 55.92	6
	MOTA	1538	CD	GLU A		41.17		23.307	1.00 56.05	6
25	MOTA	1539		GLU A		42.33		23.743	1.00 56.33	8
	MOTA	1540	_	GLU A		40.80		22.171	1.00 57.19	8
	MOTA	1541	С	GLU A		40.36		26.655	1.00 58.09	6 8
	MOTA	1542	0	GLU A		40.22		26.261	1.00 59.15	7
	MOTA	1543	N	ASP A		41.09		27.712	1.00 57.73 1.00 56.31	6
30	MOTA	1544	CA	ASP A		41.81		28.486	1.00 50.31	6
	MOTA	1545	CB	ASP A		40.85	_	29.386 30.578	1.00 57.83	6
	MOTA	1546	CG	ASP A		40.33		30.578	1.00 55.87	8
	MOTA	1547		ASP A		39.12 41.15		31.494	1.00 58.60	8
25	MOTA	1548		ASP A		42.88		29.333	1.00 55.87	6
35	MOTA	1549 1550	C	ASP A		42.74		29.714	1.00 56.72	8
	ATOM	1551	N O	VAL A		43.94		29.611	1.00 55.00	7
	ATOM ATOM	1552	CA	VAL A		45.03		30.431	1.00 55.58	6
	ATOM	1553	CB	VAL A		46.39		29.876	1.00 54.15	6
40	ATOM	1554		VAL A		47.50		30.860	1.00 52.00	6
40	MOTA	1555		VAL A		46.64		28.544	1.00 53.83	6
	ATOM	1556	C	VAL A		44.90	_	31.832	1.00 57.46	6
	ATOM	1557	ō	VAL A		44.80		32.011	1.00 57.93	8
	ATOM	1558	N	GLU A		44.88	6 14.206	32.828	1.00 58.46	7
45	MOTA	1559	CA	GLU A		44.76	7 14.654	34.204	1.00 58.24	6
	MOTA	1560	CB	GLU A	196	43.80	5 13.758	34.966	1.00 59.77	6
	MOTA	1561	CG	GLU A	. 196	43.55		36.385	1.00 63.27	6
	MOTA	1562	CD	GLU A	. 196	42.62		37.114	1.00 64.52	6
	MOTA	1563	OE1	GLU A	. 196	41.48		36.646	1.00 63.73	8
50	ATOM	1564	OE2	GLU A	. 196	43.03		38.155	1.00 68.58	8
	MOTA	1565	С	GLU A		46.14			1.00 57.57	6
	MOTA	1566	0	GLU A		46.77			1.00 59.03	8
	MOTA	1567	N	VAL A		.46.61			1.00 55.78	7
	MOTA	1568	CA	VAL A		47.92			1.00 55.65	6
55	MOTA	1569	CB	VAL A		48.78			1.00 55.24	6
	MOTA	1570		VAL A		50.14			1.00 51.21	6
	MOTA	1571		VAL A		48.92				6 6
	ATOM	1572		VAL A		47.73				8
60	MOTA	1573	0	VAL A		46.96 48.35				7
60	MOTA	1574		SER A		48.22				6
	MOTA	1575	CA	SER A	. T30	40.24		55.077		~

PCT/EP01/01457

						-90				_
	MOTA	1576	CB	SER A	198	47.951	13.822		1.00 56.54	6
	ATOM	1577	OG	SER A		46.654	13.401		1.00 61.46	8
	ATOM	1578	C	SER A		49.501	15.765	40.257	1.00 58.27	6
	ATOM	1579	ō	SER A		50.585	15.202	40.089	1.00 58.63	8
5	ATOM	1580		LEU A		49.366	16.901	40.929	1.00 58.53	7
O	ATOM	1581	CA	LEU A		50.521	17.538	41.531	1.00 60.77	6
		1582	CB	LEU A		50.519	19.046	41.274	1.00 60.73	6
	MOTA			LEU A		51.591	19.833	42.032	1.00 59.19	6
	MOTA	1583	CG	LEU A		52.982	19.400	41.599	1.00 57.61	6
4.0	MOTA	1584				51.390	21.311	41.776	1.00 60.66	6
10	MOTA	1585		LEU A		50.524	17.293	43.022	1.00 61.78	6
	MOTA	1586	С	LEU A			17.895	43.765	1.00 62.31	8
	MOTA	1587	0	LEU A		49.739		43.457	1.00 61.40	7
	MOTA	1588	N	ASN A	200	51.397	16.389	44.866	1.00 58.00	6
	MOTA	1589	CA	ASN A		51.519	16.092		1.00 60.46	6
15	MOTA	1590	CB	ASN A		51.763	14.607	45.088		6
	MOTA	1591	CG	ASN A	200	51.926	14.267	46.553	1.00 61.99	8
	MOTA	1592		ASN A		51.158	14.735	47.391	1.00 63.14	
	MOTA	1593	ND2	ASN A	200	52.928	13.447	46.871	1.00 63.54	7
	MOTA	1594	С	ASN A	200	52.708	16.906	45.345	1.00 56.52	6
20	MOTA	1595	0	ASN A		53.859	16.664	44.957	1.00 55.31	8
	MOTA	1596	N	PHE A		52.406	17.901	46.166	1.00 55.49	7
	ATOM	1597	CA	PHE A		53.416	18.790	46.707	1.00 54.84	6
		1598	CB	PHE A		53.450	20.082	45.908	1.00 50.77	6
	MOTA	1599	CG	PHE A		52.237	20.940	46.112	1.00 47.21	6
25		1600		PHE A		52.337	22.161	46.765	1.00 46.20	6
25	MOTA			PHE A		50.985	20.513	45.678	1.00 46.31	6
	MOTA	1601		PHE A		51.205	22.942	46.984	1.00 45.24	6
	MOTA	1602				49.849	21.291	45.896	1.00 43.16	6
	MOTA	1603		PHE A		49.962	22.504	46.549	1.00 42.59	6
-00	MOTA	1604	CZ	PHE A		53.035	19.112	48.142	1.00 56.47	6
30	MOTA	1605	C	PHE A		51.956	18.748	48.610	1.00 54.75	8
	ATOM	1606	0	PHE A				48.829	1.00 58.72	7
	MOTA	1607	N	ARG A		53.927	19.811	50.207	1.00 61.75	6
	MOTA	1608	CA	ARG A		53.693	20.207		1.00 63.76	6
	MOTA	1609	CB	ARG A		54.052	19.063	51.136	1.00 65.86	6
35	MOTA	1610	CG	ARG A		55.544	18.822	51.130		6
	MOTA	1611	CD	ARG A		55.938	17.640	51.962	1.00 68.52 1.00 69.87	7
	MOTA	1612	NE	ARG A		57.383	17.466	51.916		6
	MOTA	1613	CZ	ARG A		58.013	16.409	52.405	1.00 70.56	
	ATOM	1614		ARG A		57.308	15.433	52.977	1.00 71.39	7
40	ATOM	1615	NH2	ARG A		59.340	16.332	52.315	1.00 70.56	7
	MOTA	1616	С	ARG A	202	54.579	21.406	50.556	1.00 62.74	6
	MOTA	1617	. 0	ARG A	202	55.588	21.675	49.890	1.00 62.41	8
	ATOM	1618	•	LYS A	203	54.200	22.121	51.606	1.00 63.53	7
	MOTA	1619		LYS A	203	54.983	23.256	52.044	1.00 64.89	6
45	MOTA	1620		LYS A		54.271	23.993	53.169	1.00 65.59	6
	ATOM	1621		LYS A		55.067	25.149	53.740	1.00 66.14	6
	MOTA	1622		LYS A		54.348	25.777	54.911	1.00 65.85	6
	MOTA	1623		LYS A	203	55.145	26.939	55.473	1.00 67.46	6
		1624		LYS A		55.259	28.073	54.500	1.00 68.09	7
50	MOTA	1625		LYS A	203	56.264		52.563	1.00 65.93	6
50	MOTA	1626		LYS A		56.250		53.157	1.00 66.11	8
	MOTA	1627		LYS A		57.372		52.313	1.00 69.05	7
	MOTA					58.659		52.767	1.00 71.58	6
	MOTA	1628				59.758		52.358	1.00 69.66	6
	MOTA	1629						50.839	1.00 69.91	6
55		1630				59.862		50.336		6
	MOTA	1631				61.113				6
	MOTA	1632				61.195				7
	MOTA					62.324				
	MOTA				A 204	58.544				
60	MOTA				A 204	57.769				
	ATOM	163	6 N	GLY A	A 205	59.262	21.782	54.850	1.00 /3./3	′

-98

							-99 	04 -00	56 006	1 00 7F FF	6
	MOTA	1637	CA	GLY A	205		59.215	21.592	56.296	1.00 75.55	
	MOTA	1638	С	GLY A	205		60.125	22.564	57.029	1.00 76.09	6
	ATOM	1639		GLY A			60.824	23.350	56.348	1.00 77.07	8
	MOTA	1640	OT2	GLY A	205		60.151	22.545	58.278	1.00 75.36	8
5	MOTA	1641	CB	PHE B	1		33.107	19.922	1.832	1.00 57.02	6
	MOTA	1642	CG	PHE E	3 1		32.174	20.672	0.888	1.00 58.55	. 6
	MOTA	1643	CD1	PHE E	3 1		32.670	21.495	-0.120	1.00 59.39	6
	MOTA	1644	CD2	PHE E	3 1		30.784	20.612	1.079	1.00 58.84	6
	MOTA	1645	CE1	PHE E	3 1		31.795	22.248	-0.919	1.00 59.92	6
10	MOTA	1646	CE2	PHE E	3 1		29.905	21.357	0.292	1.00 56.97	6
	ATOM	1647	CZ	PHE F			30.410	22.176	-0.707	1.00 58.52	6
	ATOM	1648	С	PHE E	3 1		35.200	18.747	2.262	1.00 56.22	6
	ATOM	1649	0	PHE E	3 1		34.732	18.314	3.311	1.00 58.27	8
	MOTA	1650	N	PHE E	3 1		33.748	17.916	0.462	1.00 54.28	7
15	ATOM	1651	CA	PHE E			34.250	19.143	1.152	1.00 55.90	6
. •	ATOM	1652	N	ASP I	3 2		36.512	18.877	2.083	1.00 55.99	7
	ATOM	1653	CA	ASP I			37.383	18.526	3.204	1.00 56.44	6
	ATOM	1654	СВ	ASP I			38.876	18.485	2.792	1.00 59.88	6
	АТОМ	1655	CG	ASP I			39.364	19.782	2.139	1.00 65.04	
20	ATOM	1656	OD1	ASP I	3 2		40.076	19.729	1.091	1.00 67.12	
	MOTA	1657		ASP I			39.042	20.860	2.684	1.00 68.18	8
	MOTA	1658	С	ASP I			37.096	19.582	4.280	1.00 55.70	
	MOTA	1659	Ö	ASP I			36.331	20.507	4.047	1.00 54.61	
	MOTA	1660	N	ARG I	в 3		37.682	19.443	5.458	1.00 55.52	
25	ATOM	1661	CA	ARG			37.441	20.380	6.556	1.00 53.72	
	ATOM	1662	СВ	ARG	_		38.114	19.838	7.806	1.00 56.23	
	ATOM	1663	CG	ARG			37.541	20.323	9.094	1.00 55.76	
	ATOM	1664	CD	ARG	_		37.772	19.269	10.139	1.00 55.83	
	ATOM	1665	NE	ARG			36.531	18.930	10.818	1.00 56.35	
30	ATOM	1666	CZ	ARG			36.233	17.708	11.220	1.00 56.91	
-	MOTA	1667		ARG			37.095	16.729	10.994	1.00 56.22	
	MOTA	1668	NH2	ARG	в 3		35.090	17.468	11.849	1.00 57.84	
	MOTA	1669	С	ARG			37.909	21.822	6.295	1.00 53.67	
	MOTA	1670	0	ARG	в 3		37.395	22.772	6.888	1.00 53.80	
35	MOTA	1671	N	ALA	в 4		38.896	21.969	5.420	1.00 52.29	
	MOTA	1672	CA	ALA	в 4		39.443	23.255	5.025	1.00 50.06	
	MOTA	1673	СВ	ALA	в 4		40.743	23.036	4.275	1.00 48.42	
	ATOM	1674	С	ALA	в 4		38.442	23.978	4.131	1.00 49.06	
	ATOM	1675	0	ALA	в 4		38.225	25.179	4.270	1.00 47.12	
40	ATOM	1676	N	ASP	в 5		37.837	23.233	3.211	1.00 49.07	
	ATOM	1677	CA	ASP	B 5		36.869	23.801	2.288	1.00 51.75	
	ATOM	1678	CB	ASP	в 5		36.345	22.748	1.299	1.00 55.02	
	ATOM	1679	CG	ASP	в 5		37.454	22.084	0.491	1.00 60.18	
	MOTA	1680	0D1	LASP	в 5		38.347	22.794	-0.039	1.00 63.04	
45	MOTA	1681	OD2	ASP	B 5		37.430	20.839	0.374	1.00 61.10	
	MOTA	1682	С	ASP	B 5		35.699	24.381	3.051	1.00 51.1	
	ATOM	1683	0	ASP	в 5		35.179	25.428	2.670	1.00 51.32	
	MOTA	1684	N	ILE	в 6	i	35.292	23.713	4.130	1.00 49.73	
	ATOM	1685		ILE	в 6	;	34.164	24.178	4.926	1.00 50.0	
50	ATOM	1686		ILE	в 6	i	33.723	23.128	5.950	1.00 51.1	
	MOTA	1687		2 ILE	в 6	5	32.472	23.610	6.678	1.00 48.6	
	MOTA	1688		1 ILE	в 6	5	33.434	21.809	5.232	1.00 53.1	
	ATOM	1689		1 ILE	в 6	5	32.881	20.712	6.121	1.00 55.0	
	MOTA	1690		ILE	в 6	5	34.448	25.480	5.653	1.00 49.9	
55	MOTA	1691		ILE		5	33.700	26.450	5.518	1.00 51.6	
	ATOM	1692		LEU		7	35.524	25.504	6.426	1.00 49.4	
	MOTA	1693		LEU	в 7	7	35.908	26.705	7.160	1.00 48.1	
	ATOM	1694		LEU	в 7	7	37.157	26.424	7.995	1.00 45.6	
	ATOM	1695				7	36.916	25.427	9.126	1.00 45.9	
60	MOTA	1696	CD	1 LEU			38.221	24.935	9.696	1.00 46.5	
	MOTA	1697	CD	2 LEU	В	7	36.081	26.086	10.191	1.00 44.5	0 6

						-100				
	ътом	1698	c :	LEU B	7	36.167	27.850	6.195	1.00 47.43	6
	ATOM ATOM	1699	_	LEU B	7	35.797	28.986	6.447	1.00 46.94	8
	ATOM	1700		TYR B	8	36.799	27.529	5.080	1.00 49.45	7
	ATOM	1701		TYR B	8	37.105	28.507	4.051	1.00 52.16	6
5	ATOM	1702	_	TYR B	8	37.800	27.821	2.877	1.00 54.75	6
U	ATOM	1703		TYR B	8	38.090	28.758	1.737	1.00 56.10	6
	ATOM	1704		TYR B	8	39.088	29.720	1.839	1.00 56.48	6
	ATOM	1705		TYR B	8	39.344	30.605	0.794	1.00 57.35	6
	ATOM	1706	CD2	TYR B	8	37.348	28.701	0.564	1.00 57.26	6
10	MOTA	1707	CE2	TYR B	8	37.592	29.581	-0.484	1.00 57.99	6
	MOTA	1708		TYR B	8	38.590	30.528	-0.364	1.00 57.33 1.00 58.94	6 8
	ATOM	1709	OH	TYR B	8	38.819	31.385	-1.408	1.00 52.55	6
	MOTA	1710	С	TYR B	8	35.858	29.234	3.537	1.00 52.33	8
	MOTA	1711	0	TYR B	8	35.867	30.460	3.387 3.249	1.00 52.22	7
15	MOTA	1712	N	ASN B		34.796	28.482	2.752	1.00 54.09	6
	MOTA	1713	CA	ASN B		33.566	29.086	2.376	1.00 56.72	6
	MOTA	1714	CB	ASN B		32.539	28.021 27.203	1.163	1.00 60.46	6
	MOTA	1715	CG	ASN B		32.963 33.966	27.509	0.512	1.00 61.72	8
-00	MOTA	1716		ASN B		32.198	26.159	0.852	1.00 61.67	7
20	MOTA	1717		ASN B		32.198	30.007	3.794	1.00 54.24	6
	MOTA	1718	C	ASN B		32.680	31.160	3.506	1.00 54.66	8
	MOTA	1719	O N	ILE B		32.829	29.503	5.013	1.00 54.21	7
	MOTA	1720 1721	N CA	ILE B		32.282	30.310	6.104	1.00 53.77	6
25	MOTA MOTA	1721	CB	ILE B		32.303	29.543	7.429	1.00 52.00	6
20	MOTA	1723	CG2		_	31.860	30.451	8.552	1.00 50.79	6
	MOTA	1724	CG1			31.389	28.323	7.339	1.00 50.43	6
	ATOM	1725		ILE E		31.531	27.371	8.498	1.00 47.56	6
	ATOM	1726	C	ILE E		33.085	31.592	6.284	1.00 55.12	6
30	MOTA	1727	ō	ILE E		32.531	32.663	6.458	1.00 56.17	8
-	ATOM	1728	N	ARG E	3 11	34.400	31.464	6.243	1.00 56.91	7
	ATOM	1729	CA	ARG E	3 11	35.297	32.595	6.386	1.00 58.48	6 6
	MOTA	1730	CB	ARG F	3 11	36.739	32.110	6.243	1.00 63.85 1.00 68.86	6
	MOTA	1731	CG	ARG I		37.799	33.170	6.434	1.00 08.80	6
35	MOTA	1732	CD	ARG I		37.917	33.493	7.917	1.00 77.74	7
	MOTA	1733	NE	ARG I		39.211	34.078	8.264 7.807	1.00 88.55	6
	MOTA	1734		ARG I		40.384	33.635	6.970	1.00 90.95	7
	MOTA	1735		ARG I	_	40.424	32.589 34.239	8.178	1.00 87.63	7
	MOTA	1736		ARG		41.518 35.030	33.639	5.306	1.00 58.49	6
40	MOTA	1737		ARG		34.905	34.825	5.584	1.00 57.34	8
	MOTA	1738		ARG	_	34.933	33.175	4.066	1.00 58.50	7
	ATOM	1739		GLN GLN		34.748	34.055	2.927	1.00 57.77	6
	MOTA	1740		GLN	_	35.147	33.329	1.653	1.00 58.35	6
45	MOTA	1741		GLN	_	36.124	34.100	0.814	1.00 62.22	6
45	MOTA	1742 1743		GLN		37.514	33.973	1.351	1.00 64.08	6
	ATOM ATOM	1744				38.011		1.501	1.00 68.35	8
	MOTA	1745				38.156		1.653	1.00 63.78	7
	MOTA	1746		GLN	_	33.366	34.633	2.720		6
50		1747		GLN		33.219		2.059		8
50	MOTA	1748		THR		32.345	33.994	3.266		7
	MOTA	1749				30.987	34.479	3.054		6
	MOTA	1750				30.101		2.468		6
•	MOTA	175		1 THR	в 13	30.100	32.247	3.350		8
55		175				30.612				6
	MOTA	175		THR		30.295				6
	ATOM			THR		29.275				8 7
	MOTA			SER		30.848				6
	MOTA		6 CA			30.247				6
60	MOTA					30.884				8
	MOTA	175	8 OG	SER	в 14	30.086	34.485	, 3.034	. 1.00 00.10	•

						-101				
	N/II/OM	1759	_	SER B	14	30.343	36.619	6.949	1.00 59.80	6
	ATOM ATOM	1760	С О	SER B	14	31.247	37.293	6.443	1.00 60.23	8
	MOTA	1761	N	ARG B	15	29.382	37.134	7.710	1.00 58.15	7
	ATOM	1762	CA	ARG B	15	29.322	38.549	8.040	1.00 55.80	6
5	MOTA	1763	CB	ARG B	15	28.271	39.239	7.183	1.00 56.87	6
•	ATOM	1764	CG	ARG B	15	28.540	39.145	5.684	1.00 60.72 .	6
	MOTA	1765	CD	ARG B	15	27.721	40.179	4.945	1.00 63.19	6
	ATOM	1766	NE	ARG B	15	28.008	41.515	5.475	1.00 67.21	7
	ATOM	1767	CZ	ARG B	15	27.307	42.616	5.196	1.00 67.82	6
10	ATOM	1768		ARG B	15	26.259	42.549	4.384	1.00 69.12	7
	MOTA	1769		ARG B	15	27.660	43.789	5.722	1.00 66.84	7
	ATOM	1770	C	ARG B	15	28.962	38.655	9.511	1.00 54.09	6
	ATOM	1771	ō	ARG B	15	27.795	38.651	9.880	1.00 55.59	8
	ATOM	1772	N	PRO B	16	29.979	38.747	10.377	1.00 51.42	7
15	ATOM	1773	CD	PRO B	16	31.405	38.751	10.015	1.00 48.17	6
. •	ATOM	1774	CA	PRO B	16	29.817	38.846	11.828	1.00 48.94	6
	ATOM	1775	CB	PRO B	16	31.256	38.950	12.328	1.00 48.44	6
	ATOM	1776	CG	PRO B	16	32.038	38.262	11.284	1.00 48.62	6
	ATOM	1777	C	PRO B	16	28.974	40.014	12.300	1.00 48.35	6
20	ATOM	1778	ō	PRO B	16	28.475	40.006	13.420	1.00 49.87	8
	ATOM	1779	N	ASP B	17	28.825	41.026	11.456	1.00 49.55	, 7
	MOTA	1780	CA	ASP B	17	28.048	42.201	11.830	1.00 51.87	6
	ATOM	1781	СВ	ASP B	17	28.638	43.469	11.204	1.00 55.73	6
	ATOM	1782	CG	ASP B	17	29.956	43.896	11.856	1.00 59.93	6
25	ATOM	1783		ASP B	17	30.158	43.598	13.062	1.00 60.57	8
	ATOM	1784		ASP B	17	30.781	44.548	11.163	1.00 61.01	8
	MOTA	1785	C	ASP B	17	26.581	42.120	11.458	1.00 51.65	6
	ATOM	1786	0	ASP B	17	_25.837	43.066	11.684	1.00 51.12	8
	ATOM	1787	N	VAL B	18	26.156	40.990	10.906	1.00 53.24	7
30	MOTA	1788	CA	VAL B	18	24.772	40.848	10.495	1.00 53.38	6
	ATOM	1789	CB	VAL B	18	24.679	40.682	8.978	1.00 52.53	6
	ATOM	1790	CG1	VAL B	18	23.238	40.628	8.551	1.00 53.33	6
	ATOM	1791	CG2	VAL B	18	25.385	41.833	8.299	1.00 52.08	6
	ATOM	1792	С	VAL B	18	24.026	39.701	11.157	1.0054.80	6
35	ATOM	1793	0	VAL B	18	24.359	38.527	10.980	1.00 57.05	8
	ATOM	1794	N	ILE B		22.999	40.062	11.913	1.00 55.38	7
	MOTA	1795	CA	ILE B	19	22.150	39.105	12.615	1.00 54.84	6
	MOTA	1796	CB	ILE B		21.128	39.899	13.493	1.00 53.97	6
	MOTA	1797	CG2	ILE B		20.177	40.699	12.612	1.00 52.99	6
40	MOTA	1798	CG1			20.354	38.963	14.414	1.00 54.58	6
	MOTA	1799	CD1	L ILE B		19.598	39.696	15.490	1.00 51.38	6
	MOTA	1800	С	ILE B		21.450	38.192	11.586	1.00 55.77	6
	MOTA	1801	0	ILE E		20.879	38.678	10.605	1.00 56.23	8
	MOTA	1802	N	PRO E		21.508	36.857	11.787	1.00 57.54	7 6
45	MOTA	1803		PRO E		22.223	36.204	12.888	1.00 57.31	-
	MOTA	1804	CA	PRO E		20.900	35.841	10.900	1.00 59.26	6
	MOTA	1805	СВ	PRO E		21.478	34.521	11.417	1.00 57.46	6
	MOTA	1806	CG	PRO E		22.657	34.935	12.235	1.00 58.77 1.00 62.02	6 6
	MOTA	1807		PRO E		19.366	35.836	10.940	1.00 62.02	8
50	MOTA	1808		PRO E		18.732	34.806	11.185	1.00 65.81	7
	MOTA	1809		THR E		18.781	36.997	10.679 10.705	1.00 69.72	6
	MOTA	1810		THR E		17.337	37.160		1.00 67.96	6
	ATOM	1811		THR E		16.974	38.658	10.971 12.367	1.00 67.30	8
	ATOM	1812		1 THR E		16.710	38.837	10.178	1.00 68.09	6
55	MOTA	1813				15.765 16.606	39.087 36.658	9.455	1.00 03.03	6
	MOTA	1814		THR F		17.000	36.942	8.315	1.00 71.83	8
	MOTA	1815		THR I		15.532	35.907	9.694	1.00 77.49	7
	MOTA	1816		GLN I		14:684	35.307	8.629	1.00 80.52	6
60	ATOM	1817				14.492	33.871	8.842	1.00 81.72	.6
00	ATOM	1818 1819				15.793	33.071	8.917	1.00 83.16	6
	MOTA	1013	CG	GIIN I		13.755	23.037			-

							-102						
		1000	an.	OT 11 T	,	22	-102 15.65	.1	31.832	9.753	1.00 8	5.69	6
	MOTA	1820		GLN E		22 22	15.42		31.032	10.976	1.00 8		8
	ATOM ATOM	1821 1822		GLN I		22	15.78		30.665	9.103	1.00 8		7
	ATOM	1823	C	GLN I		22	13.32		36.091	8.717	1.00 8	1.72	6
5	ATOM	1824		GLN I		22	12.52		35.837	9.632	1.00 8	0.46	8
•	ATOM	1825		ARG I		23	13.07	5	36.990	7.765	1.00 8		7
	ATOM	1826		ARG I		23	11.82	9	37.769	7.744	1.00 8		6
	MOTA	1827	СВ	ARG 1	В	23	10.59		36.840	7.695	1.00 8		6
	MOTA	1828	CG	ARG 1		23	10.34		36.215	6.314	1.00 8		6
10	ATOM	1829	CD	ARG 1		23	10.79		34.734	6.215	1.00 9		6 7
	MOTA	1830	NE	ARG		23	10.69		34.242	4.833 4.068	1.00 9		6
	MOTA	1831	CZ	ARG		23	9.59		34.302 34.832	4.534	1.00		7
	MOTA	1832		ARG		23 23	8.45 9.62		33.855	2.811	1.00 9		7
4 =	ATOM	1833		ARG ARG		23	11.75		38.657	8.987	1.00 8		6
15	MOTA	1834 1835	C O	ARG		23	12.73		39.137	9.476	1.00 8		8
	ATOM ATOM	1836	N	ASP		24	10.54		38.879	9.497	1.00 8	_	7
	ATOM	1837	CA	ASP		24	10.39		39.703	10.693	1.00 8		6
	MOTA	1838	СВ	ASP		24	8.97	75	40.301	10.799	1.00 8		6
20	ATOM	1839	CG	ASP		24	8.23	26	40.339	9.453	1.00		6
	MOTA	1840	OD1	ASP	В	24	8.7		40.965	8.486	1.00		8
	MOTA	1841	OD2	ASP	В	24	7.1		39.746	9.376	1.00		8
	MOTA	1842	С	ASP		24	10.6		38,798	11.891	1.00		6 8
	MOTA	1843	0	ASP		24	10.4		39.218	13.045	1.00		7
25	MOTA	1844	N	ARG		25	10.9		37.549	11.613 12.677	1.00		6
	MOTA	1845	CA	ARG		25	11.2		36.584 35.159	12.128	1.00		6
	ATOM	1846	CB	ARG		25	11.3 10.0		34.541	11.696	1.00		6
	MOTA	1847	CG	ARG ARG		25 25	10.1		33.024	11.485	1.00		6
30	MOTA	1848 1849	CD NE	ARG		25	8.9		32.371	11.140	1.00		7
30	MOTA MOTA	1850	CZ	ARG		25	8.7		31.053	11.005	1.00		6
	MOTA	1851		ARG		25	9.7		30.235	11.186	1.00		7
	MOTA	1852		ARG		25	7.5	38	30.549	10.709	1.00		7
	ATOM	1853	С	ARG		25	12.5	27	36.876	13.426		75.18	6
35	ATOM	1854	0	ARG	В	25	13.5		37.105	12.813	1.00	75.11	8
	ATOM	1855	N	PRO	В	26	12.4		36.879	14.767		71.32	7 6
	MOTA	1856	CD	PRO		26	11.2		36.885	15.569		69.54 68.20	6
	MOTA	1857	CA	PRO		26	13.6		37.134 37.298	15.617 17.007	1.00	68.04	6
40	ATOM	1858	CB	PRO		26	13.0 11.6		37.763	16.720		68.94	6
40	ATOM	1859	CG	PRO		26 26	14.5		35.917	15.572		65.66	6
	MOTA	1860		PRO PRO		26	14.1		34.832	15.183		65.23	8
	MOTA ATOM	1861 1862		VAL		27	15.8		36.093	15.956		62.13	7
	ATOM	1863		VAL		27	16.7		34.969	15.990		58.35	6
45	ATOM	1864				27	18.1	L85	35.416	15.851		57.74	6
	ATOM	1865		l VAL	В	27	19.1		34.308	16.328	1.00	54.93	6
	MOTA	1866	CG	2 VAL	В	27	18.4		35.737	14.393	1.00	54.94	6
	ATOM	1867	C	VAL	В	27	16.4		34.348	17.349		56.29	6
	MOTA	1868	0	VAL		27	16.5		35.043	18.360	1.00	56.31 54.44	8 7
50	MOTA	1869		ALA		28	16.3		33.045	17.379 18.645		52.98	6
	MOTA	1870				28	16.0		32.384 31.209	18.461		52.15	6
	MOTA	1871				28	15.0 17.3		31.203	19.262		52.73	6
	MOTA	1872		ALA		28	17.		31.004	18.782		51.86	8
==	MOTA	1873		ALA VAI		28 29	17.		32.632	20.334		51.10	7
55	MOTA MOTA	1874 1875				29	18.		32.353	21.080		49.08	6
	ATOM	1876				29	19.		33.642	21.324	1.00	49.72	6
	ATOM	1877		1 VAI		29	20.		33.323	22.140		46.43	6
	MOTA	1878	B CG	2 VAI	ъВ	29	20.	117	34.272	19.996		49.12	6
60	ATOM	1879		VAI		29	18.		31.762		_	48.65	6
	MOTA	1880	0 0	IAV	В	29	17.	731	32.301	23.161	1.00	48.71	8

						102				
				ann n	3.0	-103 19.169	30.638	22.746	1.00 50.09	7
	MOTA	1881	N	SER B	30 30	18.925		24.018	1.00 53.68	6
	MOTA	1882 1883	CA CB	SER B	30	18.587		23.817	1.00 53.36	6
	MOTA MOTA	1884	OG	SER B	30	19,653	27.845	23.180	1.00 57.88	8
5	MOTA	1885	C	SER B	30	20.201	30.150	24.823	1.00 56.00	6
•	ATOM	1886	ō	SER B	30	21.297		24.306	1.00 57.56	8
	MOTA	1887	N	VAL B	31	20.049	30.542	26.084	1.00 57.69 1.00 57.19	7 6
	MOTA	1888	CA	VAL B	31	21.175	30.752	26.980	1.00 57.13	6
	MOTA	1889	CB	VAL B	31	21.227	32.198 32.449	27.460 28.185	1.00 57.52	6
10	MOTA	1890		VAL B	31	22.536	32.449	26.288	1.00 56.64	6
	MOTA	1891		VAL B	31	21.044 21.016	29.878	28.204	1.00 57.98	6
	MOTA	1892	С	VAL B	31	19.938	29.815	28.787	1.00 59.53	8
	MOTA	1893	0	VAL B		22.101	29.232	28.611	1.00 58.26	7
4 =	MOTA	1894	N	SER B		22.069	28.356	29.765	1.00 58.30	6
15	MOTA	1895 1896	CA CB	SER B		21.806	26.914	29.298	1.00 60.26	6
	MOTA MOTA	1897	OG	SER B		21.881	25.975	30.361	1.00 61.39	8
	ATOM	1898	c	SER B	_	23.374	28.414	30.530	1.00 58.22	6
	ATOM	1899	ō	SER B		24.402	27.983	30.024	1.00 62.28	8
20	MOTA	1900	N	LEU E		23.340	28.937	31.753	1.00 56.90	7 6
	MOTA	1901	CA	LEU E		24.548	29.002	32.572	1.00 56.09 1.00 54.84	6
	MOTA	1902	CB	LEU E		24.489	30.183	33.541	1.00 55.33	6
	MOTA	1903	CG	LEU F		24.257	31.555	32.914 33.962	1.00 53.97	6
	MOTA	1904		LEU F		24.483	32.647 31.731	31.737	1.00 56.27	6
25	MOTA	1905		LEU F		25.201 24.725	27.728	33.379	1.00 55.50	6
	MOTA	1906	C	LEU F		23.770	27.220	33.950	1.00 56.54	8
	MOTA	1907	0	LEU I		25.770	27.215	33.413	1.00 55.65	7
	MOTA	1908	N CA	LYS		26.270	26.018	34.183	1.00 56.27	6
30	MOTA	1909 1910	CB	LYS		26.815	24.905	33.279	1.00 60.64	6
30	MOTA MOTA	1911		LYS		25.908	24.528	32.102	1.00 66.07	6
	ATOM	1912		LYS	_	24.552	23.965	32.566	1.00 72.18	6 6
	ATOM	1913		LYS	в 34	23.611	23.670	31.373	1.00 74.46 1.00 74.04	7
	MOTA	1914		LYS	в 34	22.303	23.068	31.799	1.00 74.04	6
35	MOTA	1915	C	LYS		27.365	26.493	35.108 34.655	1.00 55.93	8
	MOTA	1916		LYS		28.463	26.811 26.564	36.401	1.00 52.21	7
	MOTA	1917		PHE		27.079 28.086	27.045	37.336	1.00 49.54	6
	MOTA	1918				27.422	27.491	38.633	1.00 46.23	6
40	MOTA	1919				26.545		38.450	1.00 47.55	6
40	MOTA	1920) CG	1 PHE		25.230		38.035	1.00 48.89	6
	MOTA	1921 1922		2 PHE		27.056	29.968	38.603	1.00 48.56	6
	MOTA MOTA	1923		1 PHE		24.434	29.653	37.771		6
	ATOM	1924	4 CE	2 PHE	в 35	26.269		38.343	1.00 45.87	6 6
45	ATOM	192				24.958		37.926		6
	ATOM	192		PHE	в 35	29.224	26.072	37.595		8
	MOTA	192	7 0	PHE		29.020			45 45	7
	MOTA	192	8 N	ILE		30.434				6
	MOTA					31.634 32.641	26.106			6
50	MOTA					33.858			1.00 38.48	6
	MOTA			G2 ILE G1 ILE		31.966			1.00 41.05	6
	ATOM			D1 ILE		31.393			3 1.00 41.45	6
	MOTA					32.284		39.029	1.00 45.51	6
55	MOTA MOTA				_	32.977	7 25.304			8
JJ	MOTA					32.068			1.00 45.06	7
	MOTA				_	32.67				6 6
	ATOM			B ASN		34.20		_		6
	ATOM		9 C			34.90				
60				D1 ASN		34.51				
	ATOM	194	11 N	D2 ASN	в 37	35.94		31.00		

PCT/EP01/01457

							-104				
	ATOM	1942	С	ASN B		37	32,222	29.077	41.322	1.00 45.58	6
	ATOM	1943	0	ASN B		37	31.767	29.931	40.566	1.00 44.62	8
	ATOM	1944	N	ILE B		38	32.335	29.248	42.635	1.00 45.83	7
	ATOM	1945	CA	ILE B		38	31.973	30.489	43.301	1.00 47.98	6
5	MOTA	1946	CB	ILE B		38	30.781	30.287	44.214	1.00 46.41	6
	ATOM	1947	CG2	ILE E	3	38	30.510	31.550	44.976	1.00 46.45	6
	MOTA	1948	CG1	ILE E	3	38	29.567	29.905	43.356	1.00 47.23	6
	MOTA	1949	CD1	ILE E		38	28.365	29.406	44.105	1.00 48.96	6
	ATOM	1950	С	ILE E		38	33.221	30.805	44.086	1.00 50.65	6
10	MOTA	1951	0	ILE E		38	33.546	30.109	45.040	1.00 52.37	8 7
	MOTA	1952	N	LEU E		39 .	33.926	31.855	43.668	1.00 52.96 1.00 53.68	6
	MOTA	1953	CA	LEU E		39	35.207	32.214	44.264 43.157	1.00 53.00	6
	MOTA	1954	CB	LEU E		39	36.137 36.204	32.698 31.706	42.000	1.00 53.70	6
15	MOTA	1955	CG	LEU E		39	37.099	32.257	40.904	1.00 53.07	6
15	MOTA	1956		LEU E		39 39	36.718	30.364	42.510	1.00 51.88	6
	MOTA	1957 1958	CD2	LEU E		39	35.272	33.188	45.418	1.00 54.85	6
	MOTA MOTA	1959	0	LEU I		39	36.061	32.994	46.342	1.00 55.07	8
	MOTA	1960	. N	GLU I		40	34.489	34.255	45.359	1.00 55.18	7
20	MOTA	1961	CA	GLU I		40	34.509	35.220	46.446	1.00 58.32	6
_0	MOTA	1962	CB	GLU I		40	35.423	36.400	46.144	1.00 59.68	6
	MOTA	1963	CG	GLU I		40	36.879	36.041	46.018	1.00 65.11	6
	ATOM	1964	CD	GLU I	3	40	37.749	37.271	45.846	1.00 69.72	6
	MOTA	1965	OE1	GLU I	В	40	37.534	38.034	44.867	1.00 72.04	8
25	MOTA	1966	OE2	GLU I	В	40	38.648	37.477	46.693	1.00 70.63	8
	MOTA	1967	С	GLU 1		40	33.128	35.738	46.685	1.00 59.54	6
	MOTA	1968	0	GLU :		40	32.393	36.057	45.747	1.00 59.65	8 7
	MOTA	1969	N	VAL		41	32.772	35.816	47.956	1.00 60.26 1.00 58.68	6
	MOTA	1970	CA	VAL		41	31.468	36.304	48.323 48.862	1.00 59.00	6
30	MOTA	1971	CB	VAL		41	30.599	35.159 35.711	49.450	1.00 61.18	6
	MOTA	1972		VAL		41	29.318 30.279	34.186	47.740	1.00 59.58	6
	MOTA	1973		VAL		41 41	31.666	37.368	49.379	1.00 58.15	6
	MOTA	1974 1975	C O	VAL		41	32.594	37.290	50.187	1.00 56.97	8
35	MOTA MOTA	1976	N	ASN		42	30.811	38.383	49.337	1.00 58.17	7
33	MOTA	1977	CA	ASN		42	30.863	39.466	50.302	1.00 58.74	6
	ATOM	1978	СВ	ASN		42	31.609	40.673	49.730	1.00 58.84	6
	ATOM	1979	CG	ASN		42	31.962	41.702	50.795	1.00 58.68	6
	MOTA	1980		ASN	В	42	31.122	42.100	51.593	1.00 58.91	8
40	ATOM	1981		2 ASN		42	33.215	42.138	50.806	1.00 58.72	7
	ATOM	1982	С	ASN	В	42	29.412	39.823	50.577	1.00 60.60	6
	MOTA	1983	0	ASN	В	42	28.738	40.457	49.747	1.00 60.01	8 7
	MOTA	1984	N	GLU		43	28.926	39.401	51.742	1.00 61.86 1.00 62.81	6
	MOTA	1985	CA	GLU		43	27.543	39.669	52.111 53.267	1.00 62.81	6
45	MOTA	1986		GLU		43	27.117 25.640	38.760 38.871	53.591	1.00 67.01	6
	MOTA	1987	CG	GLU		43	25.152	37.779	54.525	1.00 69.52	6
	MOTA	1988		GLU L GLU		43 43	23.132	37.842	54.945	1.00 68.10	8
	ATOM	1989		2 GLU		43	25.944	36.854	54.831	1.00 70.46	8
50	MOTA MOTA	1990 1991		GLU		43	27.332	41.132	52.476	1.00 60.60	6
30	ATOM	1991		GLU		43	26.223	41.649	52.387	1.00 59.23	8
	MOTA	1993		ILE		44	28.408	41.792	52.882	1.00 60.18	7
	MOTA	1994				44	28.356	43,199	53.254	1.00 61.54	6
	MOTA	1995				44	29.674	43.669	53.910	1.00 62.98	6
55	ATOM	1996		2 ILE		44	29.601	45.172	54.183	1.00 61.14	6
J- -	MOTA	1997		1 ILE		44	29.950	42.877	55.194	1.00 63.64	6
	MOTA	1998		1 ILE	В	44	29.004	43,205	56.335	1.00 65.05	6
	MOTA	1999		ILE	В	44	28.141	44.069	52.016	1.00 62.14	6
	MOTA .~	2000		ILE		44	27.318	44.992	52.024	1.00 62.54	8
60	MOTA	2001		THR		45	28.894	43.773	50.959	1.00 60.63 1.00 59.11	7 6
	MOTA	2002	CA	THR	В	45	28.806	44.527	49.721	T.00 33.11	U

	• • • • • •									
						-105				
	3.57037	2002	OD.	מ מנוח	45	30.190	44.696	49.090	1.00 58.49	6
	ATOM	2003		THR B	45	30.749	43.403	48.815	1.00 60.11	8
	ATOM	2004		THR B		31.106	45.444	50.036	1.00 56.17	6
	MOTA	2005		THR B	45		43.894	48.688	1.00 58.30	6
_	MOTA	2006		THR B	45	27.879			1.00 58.45	8
5	MOTA	2007		THR B	45	27.555	44.521	47.675	1.00 56.14	7
	MOTA	2008	N	ASN B	46	27.450	42.660	48.933		6
	ATOM	2009	CA	ASN B	46	26.560	42.001	47.986	1.00 55.54	
	MOTA	2010	CB	ASN B	46	25.242	42.770	47.894	1.00 54.26	6
	ATOM	2011	CG	ASN B	46	24.161	42.171	48.767	1.00 56.06	6
10	ATOM	2012	OD1	ASN B	46	23.195	42.835	49.103	1.00 55.63	8
. •	ATOM	2013		ASN B	46	24.314	40.898	49.123	1.00 56.99	7
	ATOM	2014	C	ASN B	46	27.190	41.867	46.591	1.00 54.59	6
		2015	o	ASN B	46	26.589	42.228	45.574	1.00 52.67	8
	MOTA		N	GLU B	_	28.408	41.337	46.565	1.00 53.06	7
4.5	MOTA	2016		GLU B		29.141	41.131	45.330	1.00 51.52	6
15	MOTA	2017	CA			30.320	42.090	45.267	1.00 49.41	6
	ATOM	2018	CB	GLU B		29.902	43.534	45.211	1.00 51.44	6
	ATOM	2019	CG	GLU B			44.472	45.232	1.00 53.91	6
	MOTA	2020	CD	GLU B		31.084		44.862	1.00 51.27	8
	MOTA	2021		GLU B		32.183	44.015		1.00 58.92	8
20	MOTA	2022	OE2	GLU B		30.911	45.662	45.604		6
	MOTA	2023	С	GLU B	47	29.627	39.697	45.262	1.00 50.23	
	ATOM	2024	0	GLU B	47	30.100	39.150	46.245	1.00 50.97	8
	ATOM	2025	N	VAL B	48	29.509	39.090	44.091	1.00 50.68	7
	ATOM	2026	CA	VAL E	48	29.928	37.706	43.909	1.00 50.46	6
25	ATOM	2027	CB	VAL E		28.712	36.793	43.633	1.00 49.57	6
	ATOM	2028		VAL E		29.162	35.370	43.440	1.00 53.01	6
		2029		VAL E		27.749	36.861	44.781	1.00 50.46	6
	MOTA		C	VAL E		30.910	37.554	42.757	1.00 49.70	6
	ATOM	2030		VAL E		30.785	38.204	41.727	1.00 50.33	8
-00	MOTA	2031	0		_	31.891	36.688	42.950	1.00 48.84	7
30	MOTA	2032	N	ASP E		32.888	36.414	41.935	1.00 49.56	6
	MOTA	2033	CA	ASP E			36.610	42.514	1.00 51.66	6
	MOTA	2034	CB	ASP I		34.283		41.456	1.00 50.41	6
	MOTA	2035	CG	ASP F		35.320	36.772	40.443	1.00 52.66	8
	MOTA	2036		ASP I		35.214	36.073		1.00 51.65	8
35	ATOM	2037	OD2	ASP I		36.240	37.586	41.639	1.00 31.03	6
	ATOM	2038	С	ASP 1	в 49	32.648	34.949	41.590		
	ATOM	2039	0	ASP I	в 49	32.973	34.052	42.364	1.00 49.38	8
	MOTA	2040		VAL	B 50	32.078	34.720	40.416	1.00 49.68	7
	ATOM	2041		VAL	в 50	31.721	33.381	39.982	1.00 48.91	6
40	MOTA	2042		VAL		30.168	33.242	40.000	1.00 50.39	6
40	ATOM	2043		VAL		29.565	33.968	38.807	1.00 47.68	6
		2043		VAL		29.767	31.781	40.006	1.00 52.12	6
	ATOM	2044		VAL		32.241	32.978	38.598	1.00 47.99	6
	MOTA					32.533	33.824	37.758	1.00 48.54	8
4-	MOTA	2046		VAL			31.669		1.00 45.73	7
45	MOTA	2047		VAL			31.091	37.116	1.00 44.16	6
	ATOM	2048		VAL		32.802	30.178	37.313	1.00 43.78	6
	MOTA	2049	CB	VAL		34.037		36.031	1.00 40.41	6
	MOTA	2050		l VAL		34.324		_	1.00 40.89	6
	MOTA	2051	L CG	2 VAL	B .51	35.245	31.005			6
50	ATOM	2052	2 C	VAL	B 51	31.673		36.569	1.00 45.01	
	MOTA	2053	3 0	VAL	B 51	31.075		37.318	1.00 48.28	8
	ATOM	2054		PHE		31.382	30.328	35.275	1.00 42.51	7
		2059				30.307	29.535	34.708	1.00 41.24	6
	MOTA	205				28.981			1.00 41.72	6
EE	MOTA					28.876			1.00 42.31	6
55	MOTA	205				28.448				6
	MOTA	205		1 PHE	B 52					6
	MOTA			2 PHE						6
	MOTA		0 CE	1 PHE	B 52					6
	MOTA ·	206		2 PHE						6
60	MOTA	206	2 CZ							
	ATOM		3 C	PHE	B 52	30.463	29.345	33.217	1.00 43.44	6

							-106				
	ATOM	2064	0	PHE I	3	52	31.264	30.008	32.585	1.00 46.26	8
	ATOM	2065		TRP I		53	29.692	28.428	32.655	1.00 44.90	7
	ATOM	2066		TRP 1		53	29.725	28.188	31.223	1.00 47.46	6
	ATOM	2067		TRP		53	29.655	26.698	30.907	1.00 47.31	6
5	MOTA	2068	CG	TRP		53	30.869	25.949	31.278	1.00 49.36	6
-	ATOM	2069		TRP		53	31.029	24.535	31.246	1.00 50.82	6
	ATOM	2070		TRP		53	32.342	24.253	31.686	1.00 49.80	6
	ATOM	2071		TRP	В	53	30.189	23.473	30.887	1.00 51.30	6
	ATOM	2072	CD1	TRP	В	53	32.057	26.463	31.719	1.00 50.05	6
10	ATOM	2073	NE1	TRP	В	53	32.947	25.448	31.968	1.00 50.43	7
	ATOM	2074	CZ2	TRP	В	53	32.835	22.955	31.779	1.00 50.23	6
	ATOM	2075	CZ3	TRP	В	53	30.676	22.182	30.977	1.00 49.78	6
	ATOM	2076	CH2	TRP	В	53	31.990	21.932	31.421	1.00 50.88	6
	MOTA	2077	С	TRP		53	28.516	28.860	30.619	1.00 48.93	6
15	MOTA	2078	0	TRP		53	27.388	28.490	30.912	1.00 48.69	8
	MOTA	2079	N	GLN		54	28.746	29.846	29.770	1.00 50.46	7
	MOTA	2080	CA	GLN		54	27.643	30.543	29.155	1.00 51.66	6 6
	MOTA	2081	CB	GLN		54	28.036	31.984	28.844	1.00 51.35 1.00 53.49	6
	ATOM	2082	CG	GLN		54	26.871	32.851	28.407	1.00 57.50	6
20	MOTA	2083	CD	GLN		54	27.117	34.326	28.693 29.837	1.00 57.95	8
	MOTA	2084	_	GLN		54	27.399	34.711	29.837	1.00 57.95	7
	ATOM	2085		GLN		54	27.016	35.161 29.790	27.898	1.00 50.04	6
	ATOM	2086	C	GLN		54	27.273 27.564	30.209	26.786	1.00 54.42	8
O.E.	ATOM	2087	0	GLN		54	26.638	28.650	28.101	1.00 52.78	7
25	MOTA	2088	N	GLN		55	26.203	27.793	27.017	1.00 53.84	6
	ATOM	2089	CA	GLN GLN		55 55	25.672	26.501	27.623	1.00 58.14	6
	ATOM	2090	CB	GLN		55	24.985	25.549	26.663	1.00 66.74	6
	MOTA	2091 2092	CG CD	GLN		55	24.756	24.190	27.315	1.00 70.87	6
30	ATOM ATOM	2092	OE1			55	24.456	24.108	28.528	1.00 73.46	8
30	ATOM	2093		GLN		55	24.897	23.117	26.527	1.00 69.32	7
	ATOM	2095	C	GLN		55	25.145	28.495	26.168	1.00 51.37	6
	ATOM	2096	Ö	GLN		55	23.993	28.631	26.563	1.00 52.24	8
	ATOM	2097	N	THR		56	25.558	28.935	24.989	1.00 48.92	7
35	ATOM	2098	CA	THR		56	24.690	29.660	24.083	1.00 47.03	6
•	ATOM	2099	СВ	THR		56	25.307	31.018	23.741	1.00 47.18	6
	ATOM	2100		THR	В	56	25.758	31.647	24.946	1.00 46.91	8
	ATOM	2101	CG2	THR	В	56	24.291	31.909	23.056	1.00 45.50	6
	ATOM	2102	С	THR	В	56	24.466	28.896	22.787	1.00 46.66	6
40	MOTA	2103	0	THR	В	56	25.351	28.202	22.306	1.00 46.60	8
	MOTA	2104	N	THR	В	57	23.273	29.034	22.220	1.00 45.86	7
	MOTA	2105	CA	THR		57	22.942	28.350	20.984	1.00 44.53	6 6
	MOTA	2106	CB	THR		57	22.320	26.958	21.247	1.00 44.84 1.00 41.11	8
4-	MOTA	2107	OG1			57	23.271	26.115	21.910 19.936	1.00 46.63	6
45	ATOM	2108	CG2		_	57	21.942	26.306 29.152	20.162	1.00 43.27	6
	ATOM	2109	С	THR		57	21.967 21.106	29.132	20.700	1.00 44.01	8
	MOTA	2110	0	THR		57	22.122	29.025	18.849	1.00 41.40	7
	MOTA	2111		TRP		58 58	21.235	29.792	17.945	1.00 42.18	6
50	MOTA	2112		TRP TRP		58	21.200	31.302	17.968	1.00 40.63	6
50	MOTA	2113 2114		TRP		58	22.800	31.729	17.377	1.00 40.64	6
	MOTA	2114		TRP		58	24.048	31.827	18.054	1.00 37.47	6
	ATOM ATOM	2116		TRP		58	24.998	32.252	17.113	1.00 37.44	6
	MOTA	2117		TRP		58	24.456	31.594	19.371	1.00 37.69	6
55	ATOM	2118		TRP		58	23.036	32.088	16.087	1.00 39.23	6
33	ATOM	2119		L TRP		58	24.354	32.404	15.917	1.00 36.19	7
	MOTA	2120		2 TRP		58	26.336	32.452	17.444		6
	ATOM	2121		3 TRP		58	25.778	31.789	19.701		6
	ATOM	2122		2 TRP		58	26.708	32.215	18.742		6
60	MOTA	2123		TRP		58	21.430	29.217	16.561		6
	MOTA	2124	0	TRP	В	58	22.226	28.320	16.383	1.00 44.24	8

and the second control of the second control

PCT/EP01/01457

						-107				
	ATOM	2125	N	SER B	59	20.711	29.729	15.579	1.00 47.57	7
	ATOM	2126	CA	SER B	59	20.814	29.181	14.246	1.00 50.36	6
	ATOM	2127	CB	SER B	59	19.517	28.410	13.937	1.00 52.43	6
	MOTA	2128	OG	SER B	59	19.677	27.455	12.901	1.00 58.14	8
5	MOTA	2129	С	SER B		21.073	30.250	13.191	1.00 51.80	6
	MOTA	2130	0	SER B		20.440	31.307	13.184	1.00 48.66	8
	MOTA	2131		ASP B		22.018	29.954	12.303	1.00 53.93	7
	MOTA	2132	CA	ASP B		22.393	30.844	11.206	1.00 56.01 1.00 57.13	6 6
40	MOTA	2133	СВ	ASP B		23.766	31.462 32.503	11.474 10.437	1.00 57.13	6
10	MOTA	2134	CG	ASP B		24.163 23.714	32.413	9.275	1.00 56.08	8
	MOTA	2135		ASP B		24.952	33.407	10.786	1.00 59.82	8
	ATOM	2136		ASP B		22.453	29.976	9.953	1.00 57.25	6
	ATOM	2137	C	ASP B		23.458	29.315	9.683	1.00 57.02	8
15	ATOM ATOM	2138 2139	O N	ARG E		21.370	29.979	9.192	1.00 59.51	7
13	ATOM	2140	CA	ARG E		21.281	29.171	7.981	1.00 62.14	6
	ATOM	2141	CB	ARG E		19.852	29.202	7.418	1.00 65.88	6
	ATOM	2142	CG	ARG E		18.842	28.288	8.125	1.00 71.80	6
	ATOM	2143	CD	ARG E		17.562	28.189	7.282	1.00 79.30	6
20	ATOM	2144	NE	ARG E	61	16.561	27.245	7.806	1.00 85.93	7
	ATOM	2145	cz	ARG E	61	15.393	26.967	7.210	1.00 88.02	6
	MOTA	2146	NH1	ARG E	61	15.059	27.553	6.059	1.00 89.55	7
	ATOM	2147	NH2	ARG E	61	14.550	26.101	7.762	1.00 88.72	7
	MOTA	2148	С	ARG E	61.	22.256	29.537	6.868	1.00 61.20	6
25	MOTA	2149	0	ARG E		22.488	28.725	5.972	1.00 61.95 1.00 59.72	8 7
	MOTA	2150	N	THR E		22.819	30.742	6.898	1.00 59.72	6
	MOTA	2151	CA	THR I	_	23.755	31.133	5.846	1.00 53.33	6
	MOTA	2152	CB	THR E		24.072	32.653 32.981	5.878 7.077	1.00 62.67	8
-00	MOTA	2153		THR I		24.790 22.783	33.461	5.826	1.00 61.46	6
30	ATOM	2154	CG2			25.055	30.355	5.992	1.00 58.40	6
	MOTA	2155	C	THR I		25.923	30.410	5.129	1.00 58.95	8
	MOTA	2156 2157	N	LEU I		25.176	29.626	7.095	1.00 57.74	7
	MOTA MOTA	2157	CA	LEU :			28.831	7.381	1.00 55.00	6
35	MOTA	2159	CB	LEU !			28.871	8.880	1.00 53.55	6
00	ATOM	2160	CG	LEU			30.230	9.531	1.00 52.72	6
	MOTA	2161		LEU			30.070	11.038	1.00 53.77	6
	ATOM	2162		LEU		28.141	30.866	8.929	1.00 52.77	6
	ATOM	2163	С	LEO :	в 63	26.163	27.377	6.971	1.00 54.84	6
40	ATOM	2164	0	LEU	в 63		26.624	6.858	1.00 55.28	8
	MOTA	2165	N	ALA	в 64		26.986	6.767	1.00 53.09	7
	ATOM	2166	CA	ALA			25.621	6.403	1.00 54.25 1.00 54.84	6 6
	MOTA	2167	CB	ALA			25.474	6.274	1.00 54.35	6
	MOTA	2168	С	ALA			25.173	5.116 4.208	1.00 56.81	8
45	MOTA	2169	0	ALA			25.973 23.884	5.040	1.00 50.85	7
	MOTA	2170	N	TRP			23.305	3.851	1.00 50.36	6
	MOTA	2171	CA	TRP TRP			23.449	3.895	1.00 47.85	6
	ATOM	2172	CB	TRP			22.496	4.836	1.00 44.59	6
50	MOTA	2173 2174	CG	TRP			22.704	6.229	1.00 42.42	6
50	MOTA MOTA	2175	CES	TRP	B 65		21.535	6.711	1.00 41.31	6
	ATOM	2176	CE				23.766	7.115	1.00 39.86	6
	MOTA	2177		TRP			21.247	4.544	1.00 43.65	6
	MOTA	2178	NE:	LTRP	в 65		20.664	5.662	1.00 42.95	7
55	MOTA	2179	CZ	2 TRP	B 65		21.393	8.041	1.00 41.27	6
	ATOM	2180	ÇZ:	3 TRP	B 6		23.624	8.439	1.00 39.24	6
	MOTA	2181		2 TRP	B 6		22.445		1.00 40.26	6
	ATOM	2182		TRP			21.835		1.00 51.92	6
	MOTA	2183		TRP			21.312		1.00 51.65 1.00 54.28	8 7
60	MOTA	2184		ASN			21.173			6
	MOTA	2185	CA	ASN	B 6	6 25.579	19.760	2.599	1.00 30.00	J

						-108				
	ATOM	2186	СВ	ASN B	66	25.361	19.349	1.139	1.00 59.16	6
	MOTA	2187	CG	ASN B	66	25.067	17.869	1.006	1.00 62.92	6
	MOTA	2188	OD1	ASN B	66	25.084	17.308	-0.090	1.00 64.20	8
	MOTA	2189	ND2	ASN B	66	24.792	17.223	2.138	1.00 63.82	7
5	MOTA	2190	С	ASN B	66	26.684	18.903	3.197	1.00 56.22	6
	MOTA	2191	0	ASN B	66	27.826	18.942	2.747	1.00 54.74	8
	MOTA	2192	N	SER B	67	26.336	18.112	4.200	1.00 57.45	7
	ATOM	2193	CA	SER B	67	27.323	17.276	4.866	1.00 60.21	6
	MOTA	2194	СВ	SER B	67	27.251	17.503	6.376	1.00 60.70	6
10	ATOM	2195	OG	SER B	67	25.956	17.197	6.844	1.00 59.26 1.00 60.90	8 6
	MOTA	2196	C	SER B	67	27.139	15.796	4.554 5.221	1.00 50.30	8
	MOTA	2197	0	SER B	67	27.705 26.350	14.926 15.519	3.528	1.00 62.89	7
	ATOM	2198	N	SER B	68 68	26.094	14.148	3.129	1.00 64.44	6
15	MOTA	2199 2200	CA CB	SER B	68	25.141	14.127	1.933	1.00 64.07	6
13	ATOM ATOM	2200	OG	SER B	68	25.569	15.023	0.923	1.00 65.05	8
	ATOM	2201	C	SER B	68	27.399	13.437	2.790	1.00 65.22	6
	ATOM	2202	Ö	SER B	68	27.491	12.215	2.898	1.00 65.18	8
	ATOM	2204	N	HIS B	69	28.414	14.203	2.401	1.00 66.21	7
20	MOTA	2205	CA	HIS B	69	29.702	13.617	2.054	1.00 66.70	6
	MOTA	2206	CB	HIS B	69	29.832	13.502	0.539	1.00 69.64	6
	ATOM	2207	CG	HIS B	69	29.047	12.363	-0.025	1.00 74.89	6
	ATOM	2208		HIS B	69	29.433	11.123	-0.417	1.00 76.05	6
	ATOM	2209	ND1	HIS B	69	27.673	12.393	-0.143	1.00 76.35	7
25	MOTA	2210	CE1	HIS B	69	27.245	11.221	-0.583	1.00 76.49	6
	MOTA	2211	NE2	HIS B	69	28.293	10.433	-0.757	1.00 76.65	7
	MOTA	2212	С	HIS B	69	30.895	14.352	2.633	1.00 65.56	6
	MOTA	2213	0	HIS B	69	31.919	14.538	1.971	1.00 63.93	8
	MOTA	2214	N	SER B	70	30.746	14.737	3.897	1.00 65.07	7 6
30	MOTA	2215	CA	SER B	70	31.772	15.463	4.632	1.00 63.00 1.00 61.97	6
	MOTA	2216	CB	SER B	70	31.954	16.854 17.393	4.004 3.551	1.00 51.37	8
	MOTA	2217	OG	SER B	70	30.716 31.353	15.576	6.105	1.00 53.22	6
	ATOM	2218	C	SER B	70 70	30.288	15.077	6.507	1.00 62.73	8
35	MOTA	2219 2220	0	SER B PRO B	71	32.204	16.199	6.937	1.00 62.42	7
33	MOTA	2221	N CD	PRO B	71	33.624	16.490	6.672	1.00 61.13	6
	MOTA	2222	CA	PRO B	71	31.901	16.371	8.361	1.00 61.29	6
	ATOM ATOM	2223	CB	PRO B	71	33.124	17.103	8.879	1.00 61.30	6
	ATOM	2224	CG	PRO B	71	34.214	16.490	8.063	1.00 60.40	6
40	ATOM	2225	c	PRO B	71	30.619	17.159	8.575	1.00 61.12	6
	ATOM	2226	ō	PRO B	71	30.222	17.964	7.733	1.00 60.52	8
	ATOM	2227	N	ASP B	72	29.973	16.916	9.708	1.00 62.69	7
	ATOM	2228	CA	ASP B	72	28.714	17.587	10.046	1.00 62.55	6
	MOTA	2229	CB	ASP B	72	27.839	16.649	10.883	1.00 64.34	6
45	MOTA	2230	CG	ASP B		27.143	15.613	10.040	1.00 67.53	6
	MOTA	2231		L ASP B		25.937		9.767	1.00 67.60 1.00 70.97	8 8
	MOTA	2232	OD2	2 ASP B		27.808	14.627	9.631	1.00 70.97	6
	MOTA	2233	C	ASP B		28.962	18.858	10.827	1.00 58.20	8
	MOTA	2234		ASP B	_	28.137	19.780	10.815 11.483	1.00 58.87	7
50	MOTA	2235		GLN B		30.123 30.549	18.883 19.981	12.339	1.00 58.03	6
	ATOM	2236		GLN B		30.400	19.583	13.788	1.00 60.56	6
	MOTA	2237		GLN B	_	29.025	19.532	14.346	1.00 62.56	6
	MOTA	2238 2239		GLN E		29.025		15.763	1.00 64.10	6
55	MOTA MOTA	2239		1 GLN E		29.599		16.003	1.00 67.42	8
55	MOTA	2240		2 GLN E		28.628		16.711	1.00 65.84	7
	MOTA	2242		GLN E		31.998		12.165	1.00 55.43	6
	MOTA	2243		GLN E		32.845		11.754	1.00 56.41	8
	MOTA	2244		VAL E		32.275		12.522	1.00 50.91	7
60	ATOM	2245				33.621		12.464	1.00 48.23	6
	MOTA	2246		VAL F	3 74	33.925	22.849	11.107	1.00 46.99	6

							-109				
	2001	2247	CG1 V	מ זמז	7	4	34.009	21.782	10.026	1.00 48.63	6
	MOTA	2247 2248		VAL B		4	32.864		10.777	1.00 45.41	6
	MOTA MOTA	2249		VAL B		4	33.734	23.259	13.532	1.00 46.89	6
	MOTA	2250	-	VAL B		14	32.731	23.812	13.964	1.00 46.87	8
5	MOTA	2251		SER B		75	34.951	23.524	13.980	1.00 44.18	7
	ATOM	2252		SER B		75	35.177	24.551	14.982	1.00 41.30	6
	ATOM	2253		SER B		75	36.314	24.145	15.920	1.00 39.05	6
	MOTA	2254		SER B		75	35.850	23.290	16.932	1.00 30.94	8
	MOTA	2255		SER B	7	75	35.513	25.856	14.264	1.00 40.02	6
10	ATOM	2256	0	SER B		75	36.478	25.936	13.516	1.00 39.74	8
	MOTA	2257	N '	VAL B		76	34.701	26.875	14.497	1.00 39.53	7 6
	MOTA	2258		VAL B		76	34.885	28.167	13.861	1.00 40.26 1.00 42.73	6
	MOTA	2259		VAL B		76	33.607	28.580	13.124	1.00 42.73	6
	MOTA	2260		VAL B		76	33.788	29.928	12.483	1.00 40.50	6
15	MOTA	2261		VAL B		76	33.244	27.539	12.090 14.861	1.00 40.57	6
	MOTA	2262	_	VAL E		76	35.218	29.256	15.926	1.00 41.80	8
	MOTA	2263		VAL B		76	34.626	29.322 30.120	14.541	1.00 40.43	7
	MOTA	2264	N	PRO E		77	36.188 37.176	30.120	13.460	1.00 39.25	6
00	MOTA	2265	CD	PRO E		77 77	36.527	31.189	15.479	1.00 39.73	6
20	MOTA	2266		PRO E		77 77	37.717	31.853	14.816	1.00 40.77	6
	MOTA	2267		PRO E		77	38.342	30.728	14.078	1.00 40.80	6
	ATOM	2268	CG C	PRO E		77	35.346	32.141	15.622	1.00 38.02	6
	MOTA	2269 2270	0	PRO E		, , 77	34.663	32.438	14.658	1.00 39.36	8
25	ATOM ATOM	2271	N	ILE E		78	35.105	32.600	16.835	1.00 37.63	7
25	ATOM	2272	CA	ILE E		78	34.018	33.515	17.129	1.00 39.61	6
	MOTA	2273	CB	ILE I		78	34.107	33.946	18.602	1.00 41.86	6
	ATOM	2274		ILE I		78	33.311	35.183	18.861	1.00 40.86	6
	ATOM	2275	CG1			78	33.622	32.799	19.469	1.00 45.04	6
30	ATOM	2276	CD1			78	32.313	32.232	18.983	1.00 46.64	6
-	ATOM	2277	C	ILE 3	В	78	34.000	34.741	16.231	1.00 41.00	6
	ATOM	2278	0	ILE 1	В	78	32.947	35.225	15.846	1.00 41.00	8 7
	MOTA	2279	N	SER 1	В	79	35.185	35.227	15.898	1.00 43.87 1.00 44.52	6
	MOTA	2280	CA	SER :		79	35.368	36.399	15.047	1.00 44.32	6
35	MOTA	2281	CB	SER		79	36.842	36.792	15.061 14.696	1.00 49.85	8
	MOTA	2282	OG	SER		79	37.657	35.687	13.593	1.00 43.47	6
	MOTA	2283	С	SER		79	34.914	36.244 37.228	12.876	1.00 43.49	8
	MOTA	2284		SER		79	34.805 34.656	35.016	13.160	1.00 43.24	7
4.0	MOTA	2285	N	SER		80	34.227	34.769	11.793	1.00 44.14	6
40	MOTA	2286		SER		80 80	34.955	33.552	11.221	1.00 44.85	6
	ATOM	2287		SER SER		80	36.354	33.781	11.115	1.00 52.06	8
	MOTA	2288		SER		80	32.731	34.545	11.690	1.00.44.49	6
	ATOM	2289		SER		80	32.213	34.308	10.609	1.00 44.54	8
45	MOTA	2290 2291		LEU		81	32.039	34.625	12.820	1.00 45.89	7
45	ATOM	2291		LEU		81	30.589	34.418	12.858	1.00 45.78	6
	MOTA MOTA	2293		LEU		81	30.250	33.187	13.700	1.00 42.48	6
	ATOM	2294		LEU		81	30.945	31.867	13.420		6
	ATOM	2295		LEU		81	30.769	30.949	14.584	1.00 41.27	6
50	MOTA	2296	CD2	LEU	В	81	30.379		12.165		6
00	ATOM	2297		LEU		81	29.909		13.513		6
	ATOM	2298		LEU		81	30.562	36.439			8
	ATOM	2299		TRP		82	28.596		13.344		7
	ATOM	2300		TRP		82	27.829		13.984		6
55	ATOM			TRP	В	82	26.493	36.962			6
	ATOM			TRP		82	25.535				6 6
	MOTA		3 CD			82	24.580		15.072		
	ATOM		4 CE	2 TRP	В	82	23.972				
	MOTA			3 TRP	В	82	24.185				
60	MOTA			1 TRP	В	82	25.459				
	MOTA	230	7 NE	1 TRP	В	82	24.527	39.490	15.138	, 1.00 41.40	,

						-11	0					
	ATOM	2308	C7.2	TRP B	82	22.5		38.238	16.671	1.00 4	2.94	6
	ATOM	2309		TRP B	82	23.			16.442	1.00 4		6
	ATOM	2310		TRP B	82	22.			17.036	1.00 4	12.57	6
	ATOM	2311		TRP B	82	27.		36.100	15.323	1.00 3	39.43	6
5	ATOM	2312		TRP B	82	27.			15.410	1.00 4	11.05	8
J	ATOM	2313		VAL B	83	27.		36.892	16.373	1.00 4	41.18	7
	ATOM	2314		VAL B	83	27.		36.359	17.699	1.00 4	10.57	6
	ATOM	2315	CB	VAL B	83	28.		36.210	18.444	1.00 4	41.00	6
	ATOM	2316		VAL B	83			35.956	19.903	1.00 4	45.57	6
10	ATOM	2317		VAL B	83			35.066	17.856	1.00 4	40.97	6
10	ATOM	2318		VAL B	83			37.275	18.460	1.00	40.40	6
	ATOM	2319	Ö	VAL B	83	26.	424	38.487	18.301	1.00	42.78	8
	ATOM	2320	N	PRO B	84	25.	510	36.693	19.271	1.00	40.62	7
	ATOM	2321	CD	PRO B	84	25.	296	35.250	19.465	1.00		6
15	ATOM	2322	CA	PRO B		24.	540	37.460	20.052	1.00		6
.0	ATOM	2323	CB	PRO B		23.	839	36.384	20.880	1.00		6
	ATOM	2324	CG	PRO B		23.	899	35.212	20.013	1.00		6
	ATOM	2325	C.	PRO B		25.	246	38.474	20.937	1.00		6
	MOTA	2326	ō	PRO B		26.	215	38.140	21.603	1.00		8
20	ATOM	2327	N	ASP B	85	24.	753	39.706	20.950	1.00		7
	MOTA	2328	CA	ASP B	85	25.	341	40.736	21.777	1.00		6
	ATOM	2329	CB	ASP B	85		112	42.107	21.152		38.52	6
	ATOM	2330	CG	ASP B	85	23.	661	42.418	20.952		40.81	6
	MOTA	2331	OD1	ASP B	85	22.	.925	41.501	20.578		41.81	8
25	ATOM	2332	OD2	ASP E	85	23.	254	43.579	21.148		41.12	8
	MOTA	2333	С	ASP B	85		.776	40.687	23.193		39.08	6
	ATOM	2334	0	ASP E	85		.261	41.668	23.714		36.01	8 7
	MOTA	2335	N	LEU E	86		.902	39.522	23.811		38.19	6
	MOTA	2336	CA	LEU E	86		.421	39.306	25.161		39.63	6
30	MOTA	2337	СВ	LEU E			.459	37.819	25.502		37.18 38.33	6
	MOTA	2338	CG	LEU E			.585	36.939	24.621		33.72	6
	MOTA	2339		LEU E			.700	35.493	25.065		35.49	6
	MOTA	2340	CD2	LEU E			.159	37.433	24.693		40.05	6
	MOTA	2341	С	LEU E	_		.223	40.061	26.201		42.26	8
35	MOTA	2342	0	LEU F	_		.432	40.251	26.065		40.28	7
	MOTA	2343	N	ALA I			.541	40.467	27.260 28.339		40.51	6
	MOTA	2344	CA	ALA I			.180	41.193	28.091		40.62	6
	MOTA	2345	CB	ALA 1			.048	42.698 40.826	29.660		40.28	6
	MOTA	2346	С	ALA I			.521	40.702	29.729		40.56	8
40	MOTA	2347	0	ALA I			.306	40.702	30.703		39.13	7
	MOTA	2348	N	ALA			.316	40.340	32.014		38.99	6
	MOTA	2349	CA	ALA			.749	39.577	32.850	1.00	37.09	6
	MOTA	2350	CB	ALA			.433	41.686	32.665		40.68	6
45	MOTA	2351	C	ALA ALA			.319	42.392	33.134		38.34	8
45	MOTA	2352					.153	42.033	32.667		42.45	7
	MOTA	2353	N	TYR TYR	_		.654	43.285	33.232	1.00	44.08	6
	ATOM	2354		TYR			.133	43.209	33.363	1.00	46.62	6
	ATOM	2355		TYR			395	43.055	32.056	1.00	51.23	6
EΩ	MOTA	2356 2357		1 TYR			.022	42.816	32.036		54.25	6
50	MOTA			1 TYR			3.322	42.711	30.826		55.90	6
	MOTA	2358 2359		2 TYR			1.054	43.179	30.835		52.13	6
	MOTA	2360					3.366	43.078	29.626		54.28	6
	MOTA	2361					9.001	42.847	29.629		55.97	6
55	ATOM	2362					8.313	42.787	28.440		59.26	8
55	MOTA	2362		TYR			3.243	43.725	34.579		43.48	6
	MOTA MOTA	2364		TYR			3.409	44.917	34.820		42.18	8
	MOTA	2365		ASN			3.540	42.784	35.466		42.08	7
	ATOM	2366					4.102			1.00	40.43	6
60	MOTA	2367					3.262	42.581			39.29	6
	MOTA	2368					3.084		37.824	1.00	40.77	6

						111				
					00	-111 22.778	40.536	36.774	1.00 40.90	8
	MOTA	2369		ASN B	90 90	23.257			1.00 42.41	7
	ATOM	2370		ASN B	90	25.554		36.921	1.00 41.50	6
	MOTA	2371	С	ASN B ASN B	90	26.031		38.042	1.00 42.85	8
5	MOTA	2372 2373	N O	ALA B	91	26.250			1.00 43.60	7
J	MOTA	2374	CA	ALA B	91	27.669		35.811	1.00 43.31	6
	ATOM ATOM	2375	CB	ALA B	91	28.156	41.933		1.00 42.36	6
	ATOM	2376	C	ALA B	91	28.359	43.513	36.336	1.00 44.47	6
	ATOM	2377	ō	ALA B	91	28.048	44.637	35.934	1.00 43.75	8
10	ATOM	2378	N	ILE B	92	29.295	43.299	37.244	1.00 44.99	7
. •	ATOM	2379	CA	ILE B	92	30.009	44.379	37.895	1.00 45.69	6
	MOTA	2380	CB	ILE B	92	30.052	44.061	39.418	1.00 46.91	6
	ATOM	2381	CG2	ILE B	92	31.419	43.514	39.831	1.00 49.50	6
	MOTA	2382	CG1	ILE B	92	29.726	45.288	40.232	1.00 48.64	6 6
15	MOTA	2383	CD1	ILE B	92	29.920	45.030	41.718	1.00 53.73 1.00 45.86	6
	MOTA	2384	С	ILE B	92	31.428	44.532	37.302	1.00 45.86	8
	MOTA	2385	0	ILE B	92	32.156	45.487	37.611	1.00 41.25	7
	MOTA	2386	N	SER B	93	31.804	43.581	36.453 35.813	1.00 41.23	6
	MOTA	2387	CA	SER B	93	33.104	43.578	36.568	1.00 35.19	6
20	MOTA	2388	CB	SER B	93	34.056	42.662 41.315	36.388	1.00 35.43	8
	MOTA	2389	OG	SER B	93	33.682 32.852	43.015	34.431	1.00 40.88	6
	MOTA	2390	C	SER B	93	31.776	42.493	34.174	1.00 39.63	8
	MOTA	2391	0	SER B		33.815	43.131	33.524	1.00 43.16	7
0.5	MOTA	2392	N	LYS B		33.598	42.557	32.212	1.00 43.98	6
25	MOTA	2393	CA	LYS B		34.355	43.325	31.127	1.00 46.29	6
	MOTA	2394	CB CG	LYS B		35.769	43.727	31.434	1.00 50.31	6
	MOTA	2395 2396	CD	LYS B		36,225	44.764	30.401	1.00 52.39	6
	MOTA	2397	CE	LYS E		35.853	44.341	28.978	1.00 52.02	6
30	ATOM ATOM	2398	NZ	LYS E		36.333	45.308	27.965	1.00 54.82	7
30	ATOM	2399	C	LYS E		33.963	41.075	32.230	1.00 43.71	6
	MOTA	2400	ō	LYS E		34.673	40.602	33.114	1.00 44.78	8
	ATOM	2401	N	PRO E	_	33.443	40.310	31.267	1.00 44.16	7
	MOTA	2402	CD	PRO E	3 95	32.562	40.750	30.171	1.00 42.37	6 6
35	MOTA	2403	CA	PRO E	3 95	33.704	38.873	31.184	1.00 39.82 1.00 40.83	6
-	MOTA	2404	СВ	PRO E		32.836	38.422	30.016	1.00 40.83	6
	ATOM	2405	CG	PRO I	3 95	31.813	39.505	29.881	1.00 42.30	6
	ATOM	2406	C	PRO 1		35.141	38.524	30.941 30.032	1.00 40.47	8
	MOTA	2407	0	PRO I		35.772	39.048	31.765	1.00 39.61	7
40	MOTA	2408	N	GLU 1		35.663	37.637 37.175	31.783	1.00 39.82	6
	MOTA	2409				37.020		32.915	1.00 41.36	6
	MOTA	2410				37.765 39.238		32.763	1.00 50.17	6
	MOTA	2411				39.989		34.094	1.00 55.05	6
4-	MOTA	2412			_	39.506	37.129	35.084	1.00 57.32	8
45	MOTA	2413	OE	E1 GLU		41.067		34.153	1.00 56.17	8
	MOTA	2414		GLU GLU		36.802		30.966	1.00 39.55	6
	MOTA	2415		GLU		36.537		31.676	1.00 38.71	8
	MOTA	2416		VAL		36.864		29.638	1.00 36.87	7
50	ATOM	2417 2418				36.690		28.938	1.00 35.52	6
50	MOTA MOTA	241				36.457		27.448	1.00 35.28	6
	ATOM			G1 VAL		36.249	33.378		1.00 33.50	6
	ATOM			G2 VAL		35.249				6
	ATOM					37.935			1.00 35.07	6
55						39.025				8
	ATOM				в 98	37.75				7 6
	ATOM									6
	АТОМ									6
	ATOM			G LEU						6
60	MOTA (8 C	D1 LEU	B 98					6
	ATOM	242	9 C	D2 LEU	B 98	39.30	6 32.469	, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	00 11.20	

						-1	12					
	MOTA	243Ö	С	LEU B	98	39	.198	30.581	29.128	1.00 3	6.56	6
	ATOM	2431	o	LEU B	98		.195	29.889	29.251	1.00 3	7.06	8
	ATOM	2432	N	THR B	99	38	.371	30.467	28.103	1.00 3	6.66	7
	MOTA	2433	CA	THR B	99	38	.578	29.438	27.100	1.00 3		6
5	ATOM	2434	CB	THR B	99	37	.405	28.414	27.142	1.00 4		6
_	MOTA	2435	OG1	THR B	99	36	.152	29.097	26.972	1.00 4		8
	ATOM	2436	CG2	THR B	99	37	.400	27.676	28.466	1.00 3		6
	ATOM	2437	С	THR B	99	38	.725	29.932	25.680	1.00 3		6
	ATOM	2438	0	THR B	99	38	.401	31.073	25.378	1.00 3		8
10	MOTA	2439	N	PRO B	100	39	.231	29.066	24.786	1.00 3		7
	MOTA	2440	CD	PRO B	100		.818	27.745	25.056	1.00		6
	MOTA	2441	CA	PRO B	100		.413	29.420	23.380	1.00		6
	MOTA	2442	CB	PRO B	100	39	.783	28.095	22.745	1.00		6
	MOTA	2443	CG	PRO B			.603	27.476	23.789	1.00		6
15	MOTA	2444	С	PRO B	100	38	.107	29.961	22.852	1.00		6
	MOTA	2445	0	PRO B			.052	29.396	23.103	1.00		8
	ATOM	2446	N	GLN B	101		1.168	31.066	22.130	1.00		7
	ATOM	2447	CA	GLN B			.949	31,636	21.621	1.00		6 6
	ATOM	2448	СВ	GLN B			.071	33.155	21.576	1.00		6
20	MOTA	2449	CG	GLN B			.866	33.742	22.960	1.00	_	6
	MOTA	2450	CD	GLN B			7.334	35.158	23.075	1.00		8
	ATOM	2451	OE1				5.871	36.035	22.350	1.00		7
	MOTA	2452	NE2	GLN E			3.260	35.398	23.997	1.00		6
	MOTA	2453	С	GLN E			5.536	31.057	20.295 19.282		37.88	8
25	MOTA	2454	0	GLN E			5.496	31.747	20.342	1.00		7
	MOTA	2455	N	LEU E			5.212	29.768	19.183		39.64	6
	MOTA	2456	CA	LEU E			5.770	28.997	18.982		37.23	6
	MOTA	2457	CB	LEU E			5.652	27.759	18.842		37.24	6
	MOTA	2458	CG	LEU E			3.155	27.988 26.666	18.659		33.59	6
30	MOTA	2459		LEU E			8.852		17.665		36.66	6
	MOTA	2460		LEU E			8.429 4.349		19.394		39.73	6
	MOTA	2461	C	LEU I			3.948		20.502		38.45	8
	MOTA	2462	0	LEU I			3.586		18.317		41.12	7
O.E.	ATOM	2463	N	ALA I			2.218		18.375	1.00	40.48	6
35	MOTA	2464	CA		3 103		1.271	 -	17.760		39.15	6
	MOTA	2465	CB		B 103		2.163		17.599	1.00	40.28	6
	MOTA	2466	С 0		B 103		3.109		16.917		38.52	8
	ATOM	2467 2468	N		B 104		1.045		17.715		42.85	7
40	MOTA	2469	CA		B 104		0.876		17.019	1.00	44.21	6
40	MOTA: MOTA	2470	CB		B 104		0.557		18.027		43.23	6
	ATOM	2471	CG	ARG			0.760		17.496		45.99	6
	ATOM	2472	CD		в 104	3	2.214	21.957	17.217		44.48	6
	MOTA	2473	NE		в 104	3	2.306	20.612	16.652		45.67	7
45	ATOM	2474	CZ		B 104		3.434	19.985	16.341		42.29	6
	MOTA	2475		1 ARG	в 104	3	4.593			1.00	40.18	7
	ATOM	2476	NH:	2 ARG	в 104		3.397		15.847		43.70	7
	ATOM	2477	С	ARG	B 104		9.73				44.71	6
	ATOM	2478	0		B 104		8.65				43.84	8
50	ATOM	2479	N	VAL	B 105		9.99				45.98	7
	ATOM	2480	CA		B 105		28.95				46.86	6
	MOTA	2481			в 105		29.40				43.67	6 6
	MOTA	2482		1 VAL			28.25				42.93	
	MOTA	2483	CG	2 VAL	B 105		29.88				41.79 50.58	6 6
55	MOTA	2484			B 105		28.54				51.09	8
	MOTA	2485			B 105		29.39				51.09	7
	ATOM	2486			В 106		27.24				52.00	6
	MOTA	2487			B 106		26.67				.52.31	6
	MOTA	2488			B 106		25.46			1 00	52.15	6
60	MOTA			1 VAL			25.03				50.55	6
	MOTA	2490) CG	2 VAL	B TOO		25.79	0 21.00	14.000			•

```
-113
                                                                                      26.243 22.369 11.147 1.00 52.00
                                                VAL B 106
          ATOM
                           2491 C
                                                                                 25.762
26.388 21.401
26.038 21.592
7 175 20.272
                                                                                      25.782 23.474 10.870
26.388 21.401 10.248
                                                                                                                                               1.00 52.80
                           2492 O VAL B 106
          MOTA
                                                                                                                                               1.00 51.28
                                                                                                                                                                              7
                                                   SER B 107
          MOTA
                           2493 N
                                                                                                                                               1.00 52.41
                                                                                                                                                                               6
                           2494 CA
                                                   SER B 107
                                                                                                                             8.845
          MOTA
                                                                                                                                              1.00 54.05
                                                                                                                             8.097
           MOTA
                           2495
                                        CB
                                                   SER B 107
                                                                                                                                              1.00 58.60
                                                                                                                                                                               8

      2496
      OG
      SER B 107
      25.609
      19.216
      8.855
      1.00 58.60

      2497
      C
      SER B 107
      24.676
      22.198
      8.544
      1.00 52.33

      2498
      O
      SER B 107
      24.469
      22.728
      7.460
      1.00 52.31

      2499
      N
      ASP B 108
      23.753
      22.132
      9.494
      1.00 54.48

      2500
      CA
      ASP B 108
      22.417
      22.687
      9.285
      1.00 57.36

      2501
      CB
      ASP B 108
      21.376
      21.830
      10.007
      1.00 59.13

      2502
      CG
      ASP B 108
      21.474
      21.933
      11.512
      1.00 61.77

      2503
      OD1
      ASP B 108
      22.604
      21.993
      12.034
      1.00 63.26

      2504
      OD2
      ASP B 108
      20.419
      21.993
      12.180
      1.00 63.13

      2505
      C
      ASP B 108
      22.266
      24.152
      9.715
      1.00 58.76

      2506
      O
      ASP B 108
      21.163
      24.696
      9.711
      1.00 60.28

      2507
      N
      GLY B 109
      23.376
      24.784
      10.08
                                                                                   25.609 19.216
                                                                                                                            8.855
                                                   SER B 107
           MOTA
                            2496 OG
                                                                                                                                                                               6
           MOTA
                                                                                                                                                                               8
           MOTA
                                                                                                                                                                               7
           MOTA
10
           MOTA
                                                                                                                                                                               6
           MOTA
                                                                                                                                                                               6
           MOTA
                                                                                                                                                                               8
           MOTA
                                                                                                                                                                               8
           MOTA
15
           MOTA
                                                                                                                                                                               8
                          MOTA
                                                                                                                                                                               7
            MOTA
                                                                                                                                                                               6
            MOTA
                                                                                                                                                                               6
            MOTA
20
            MOTA
                                                                                                                                                                                7
            ATOM
                                                                                                                                                                                б
            MOTA
                                                                                                                                                                                6
            MOTA
                                                                                                                                                                                6
            ATOM
                                                                                                                                                                                6
25
            MOTA
             MOTA
             MOTA
                                                                                                                                                                                6
             MOTA
             MOTA
                                                                                                                                                                                7
 30
             MOTA
             MOTA
             MOTA
                                                                                                                                                                                6
             MOTA
                                                                                                                                                                                6
             MOTA
                                                                                                                                                                                6
 35
             MOTA
             MOTA
                                                                                                                                                                                7
             MOTA
                                                                                                                                                                                6
             MOTA
                                                                                                                                                                                 6
             MOTA
                                                                                                                                                                                 6
  40
             MOTA
              MOTA
              MOTA
                                                                                                                                                                                 6
              MOTA
                                                                                                                                                                                 8
              ATOM
                                                                                                                                                                                  7
  45
              ATOM
                                                                                                                                                  1.00 46.01
                                                                                                                                                                                  6
              MOTA
                                                                                                                                                                                 6
              MOTA
                                                                                                                                                                                  6
              MOTA
                                                                                                                                                                                  6
              MOTA
                                                                                                                                                                                  6
   50
              MOTA
                                                                                                                                                                                  6
              MOTA
                                                                                                                                                                                  6
              MOTA
                                                                                                                                                                                  6
               MOTA
                                                                                                                                                                                  8
               MOTA
                                                                                                                                                                                  6
   55
              MOTA
                                                                                                                                                                                  8
               MOTA
                                                                                                                                                                                  7
               MOTA
                MOTA
                                                                                                                                                                                   6
                MOTA
   60
                MOTA
                                                                                                                                                  1.00 61.08 16
                MOTA
```

PCT/EP01/01457 WO 01/58951

```
MOTA
   MOTA
   MOTA
   MOTA
5
   MOTA
   MOTA
   MOTA
   MOTA
   MOTA
10
   MOTA
   MOTA
   MOTA
    MOTA
   MOTA
15
   MOTA
    MOTA
    MOTA
    MOTA
    ATOM.
20
    MOTA
    MOTA
    MOTA
    MOTA
    ATOM
25
    MOTA
    MOTA
    MOTA
    MOTA
    MOTA
30
   ATOM
    MOTA
    MOTA
    MOTA
    MOTA
35 ATOM
    ATOM
    MOTA
    MOTA
    MOTA
40
    MOTA
    MOTA
    MOTA
    MOTA
     MOTA
45 атом
     MOTA
     MOTA
     ATOM
     ATOM
50
     MOTA
     ATOM
     MOTA
     MOTA
     ATOM
 55
     MOTA
     MOTA
     MOTA
     MOTA
     MOTA
 60
     MOTA
     MOTA
```

					-115				
	ATOM	2613	CE1	PHE B 121	28.585	36.920	37.212	1.00 38.44	6
	MOTA	2614		PHE B 121	27.013	38.245	35.977	1.00 38.36	6
	ATOM	2615	CZ	PHE B 121	27.959	37.232	36.020	1.00 37.80	6
	ATOM	2616	С	PHE B 121	27.549	41.193	41.142	1.00 47.76	6
5	ATOM	2617	0	PHE B 121	28.094	40.972	42.224	1.00 45.87	8
	ATOM	2618	N	SER B 122	26.521	42.021	40.966	1.00 49.39	7
	ATOM	2619	CA	SER B 122	25.881	42.735	42.054	1.00 51.30	6
	MOTA	2620	CB	SER B 122	25.677	44.200	41.680	1.00 50.63	6
	MOTA	2621	OG	SER B 122	25.026	44.887	42.726	1.00 52.75	8
10	ATOM	2622	С	SER B 122	24.530	42.041	42.235	1.00 52.14	6
	MOTA	2623	0	SER B 122	23.659	42.135	41.377	1.00 51.12	8
	MOTA	2624	N	CYS B 123	24.371	41.323	43.340	1.00 53.84	7
	ATOM	2625	CA	CYS B 123	23.133	40.605	43.603	1.00 56.99	6
	ATOM	2626	С	CYS B 123	22.973	40.343	45.111	1.00 58.94	6
15	MOTA	2627	0	CYS B 123	23.837	40.727	45.911	1.00 58.00	8
	ATOM	2628	CB	CYS B 123	23.135	39.282	42.830	1.00 55.83	6
	MOTA	2629	SG	CYS B 123	24.561	38.231	43.250	1.00 57.55	16
	ATOM	2630	N	ASP B 124	21.874	39.687	45.491	1.00 59.24	7
	ATOM	2631	CA	ASP B 124	21.619	39.412	46.893	1.00 59.17	6
20	ATOM	2632	СВ	ASP B 124	20.148	39.085	47.114	1.00 61.47	6
	ATOM	2633	CG	ASP B 124	19.670	39.487	48.505	1.00 62.03	6
	ATOM	2634	OD1	ASP B 124	20.462	39.403	49.470	1.00 60.72	8
	ATOM	2635		ASP B 124	18.493	39.886	48.628	1.00 63.80	8
	MOTA	2636	С	ASP B 124	22.470	38.274	47.434	1.00 59.25	6
25	ATOM	2637	0	ASP B 124	22.309	37.122	47.036	1.00 58.84	8
	ATOM	2638	N	VAL B 125	23.365	38.612	48.356	1.00 59.36	7
	ATOM	2639	CA	VAL B 125	24.260	37.647	48.979	1.00 59.62	6
	ATOM	2640	СВ	VAL B 125	25.683	38.230	49.080	1.00 57.35	6
	ATOM	2641	CG1	VAL B 125	26.599	37.280	49.798	1.00 54.50	6
30	ATOM	2642	CG2		26.212	38.519	47.702	1.00 58.35	6
•	MOTA	2643	С	VAL B 125	23.766	37.277	50.378	1.00 62.42	6
	ATOM	2644	0	VAL B 125	24.161	36.254	50.938	1.00 64.51	8
	ATOM	2645	N	SER B 126	22.892	38.105	50.939	1.00 63.61	7
	ATOM	2646	CA	SER B 126	22.375	37.857	52.283	1.00 64.32	6
35	MOTA	2647	СВ	SER B 126	21.260	38.857	52.613	1.00 63.21	6
	ATOM	2648	OG	SER B 126	20.175	38.715	51.715	1.00 59.22	8
	ATOM	2649	С	SER B 126	21.858	36.429	52.444	1.00 64.47	6
	MOTA	2650	0	SER B 126	21.082	35.940	51.626	1.00 63.31	8
	ATOM	2651	N	GLY B 127	22.313	35.764	53.496	1.00 65.55	7
40	ATOM	2652	CA	GLY B 127	21.872	34.409	53.748	1.00 68.84	6
. •	ATOM	2653	С	GLY B 127	22.847	33.351	53.282	1.00 70.32	6
	MOTA	2654	0	GLY B 127	22.634	32.161	53.500	1.00 71.17	8
	MOTA	2655	N	VAL B 128	23.923		52.638	1.00 71.67	7
	ATOM	2656	CA	VAL B 128	24.910		52.148	1.00 72.95	6
45	MOTA	2657	CB	VAL B 128	26.107		51.467	1.00 71.97	6
. •	MOTA	2658	CG:	L VAL B 128	25.686		50.149	1.00 73.72	6
	ATOM	2659		2 VAL B 128	26.654	34.614	52.359	1.00 69.90	6
	ATOM	2660		VAL B 128	25.504		53.212	1.00 73.83	6
	ATOM	2661		VAL B 128	25.628	30.743	53.016	1.00 73.27	8
50	ATOM	2662		ASP B 129			54.332	1.00 75.83	7
	MOTA	2663		ASP B 129	26.532		55.384	1.00 78.34	6
	ATOM	2664		ASP B 129	27.008		56.504	1.00 79.36	6
	ATOM	2665		ASP B 129	28.209		57.257	1.00 81.22	6
	MOTA	2666		1 ASP B 129	29.166		57.523	1.00 81.78	8
55	MOTA	2667		2 ASP B 129	28.202		57.576		8
	MOTA	2668		ASP B 129			55.972		6
	MOTA	2669		ASP B 129	26.293		56.660		8
	ATOM	2670		THR B 130	24.412		55.706		
	MOTA	2671		THR B 130	23.640				
60	ATOM	2672	CB	THR B 130	23.683	1 29.563			
	MOTA	2673		1 THR B 130		30.862	58.195	1.00 84.93	8

PCT/EP01/01457

					-110				_
	MOTA	2674	CG2 T	HR B 130	24.582	28.416		1.00 85.83	6
	ATOM	2675		HR B 130	22.182	29.286		1.00 80.84	6
	MOTA	2676		HR B 130	21.460	30.224	55.506	1.00 78.93	8
	ATOM	2677		LU B 131	21.784	28.014	56.028	1.00 80.92	7
5	ATOM	2678		LU B 131	20.416	27.510	55.832	1.00 80.70	6
J	ATOM	2679		SLU B 131	19.435	28.339	56.689	1.00 83.05	6
	ATOM	2680		SLU B 131	19.467	28.017	58.187	1.00 84.49	6
				ELU B 131	19.024	29.189	59.051	1.00 85.34	6
	MOTA	2681		SLU B 131	17.948	29.773	58.762	1.00 86.44	8
40	MOTA	2682		SLU B 131	19.757	29.521	60.019	1.00 85.14	8
10	ATOM	2683			19.864	27.420	54.426	1.00 79.07	6
	MOTA	2684		GLU B 131		26.520	53.643	1.00 76.96	8
	MOTA	2685		GLU B 131	20.207	28.328	54.156	1.00 78.17	7
	MOTA	2686		SER B 132	18.941		52.858	1.00 77.92	6
	ATOM	2687		SER B 132	18.298	28.449	•	1.00 77.07	6
15	ATOM	2688		SER B 132	16.953	29.195	53.001	1.00 77.45	8
	MOTA	2689	OG :	SER B 132	17.130	30.486	53.575		6
	ATOM	2690		SER B 132	19.277	29.220	51.945	1.00 76.88	
	ATOM	2691	0	SER B 132	19.000	29.463	50.759	1.00 77.41	8
	MOTA	2692	N .	GLY B 133	20.424	29.588	52.520	1.00 74.38	7
20	MOTA	2693		GLY B 133	21.442	30.308	51.782	1.00 72.04	6
	ATOM	2694	С	GLY B 133	20.943	31.569	51.105	1.00 71.42	6
	MOTA	2695		GLY B 133	19.888	32.104	51.450	1.00 71.39	8
	ATOM	2696		ALA B 134	21.708	32.044	50.125	1.00 69.68	7
	ATOM	2697		ALA B 134	21.345	33.251	49.390	1.00 66.69	6
25	ATOM	2698		ALA B 134	22.534	34.194	49.315	1.00 66.34	6
20		2699		ALA B 134	20.874	32.908	47.993	1.00 64.53	6
	ATOM		0	ALA B 134	21.095	31.802	47.504	1.00 64.56	8
	MOTA	2700		THR B 135	20.207	33.865	47.369	1.00 62.63	7
	MOTA	2701		THR B 135	19.719	33.696	46.017	1.00 62.23	6
-00	MOTA	2702		THR B 135	18.205	33.577	45.980	1.00 62.17	6
30	MOTA	2703			17.812	32.456	46.775	1.00 64.85	8
	MOTA	2704		THR B 135	17.721	33.370	44.543	1.00 62.33	6 ·
	ATOM	2705		THR B 135		34.900	45.194	1.00 62.39	6
	MOTA	2706	С	THR B 135	20.159	36.009	45.308	1.00 62.56	8
	MOTA	2707	0	THR B 135	19.618	34.661	44.379	1.00 61.14	7
35	MOTA	2708	N	CYS B 136	21.174		43.526	1.00 58.61	6
	MOTA	2709	CA	CYS B 136	21.754	35.668	42.134	1.00 56.85	6
	MOTA	2710	С	CYS B 136	21.159	35.497	41.503	1.00 55.78	8
	MOTA	2711	0	CYS B 136	21.308	34.452		1.00 58.82	6
	ATOM	2712	CB	CYS B 136	23.276		43.527	1.00 60.36	16
40	ATOM	2713	SG	CYS B 136	24.201		42.315	1.00 55.98	7
	ATOM	2714	N	ARG B 137	20.453		41.670	1.00 56.14	6
	ATOM	2715	CA	ARG B 137	19.845		40.353	1.00 57.73	6
	ATOM	2716	CB	ARG B 137	18.421		40.383	1.00 57.73	6
	ATOM	2717	CG	ARG B 137	17.502		41.303	1.00 62.21	6
45	ATOM	2718	CD	ARG B 137	16.367		41.792	1.00 68.77	7
	MOTA	2719	NE	ARG B 137	15.827		43.071	1.00 74.27	
	ATOM	2720		ARG B 137	15.070		43.224	1.00 76.32	6
•	ATOM	2721		ARG B 137	14.739	34.822	42.174		7
	ATOM	2722		ARG B 137	14.652		44.434		7
50	ATOM	2723		ARG B 137	20.672	37.253	39.366		6
00	MOTA	2724		ARG B 137	21.052	38.389	39.637	1.00 57.67	8
	MOTA	2725		ILE B 138	20.933	36.646	38.215		7
		2726		ILE B 138	21.716	37.255	37.163	1.00 48.96	6
	MOTA	2727		ILE B 138	22.977			1.00 45.32	6
55	MOTA			2 ILE B 138	23.751				6
55				L ILE B 138	23.822			1.00 42.90	6
	MOTA			L ILE B 138	24.93			1.00 40.32	6
	ATOM			ILE B 138	20.863				6
	MOTA			ILE B 138	20.420				8
~~	MOTA			LYS B 139	20.62				7
60					19.82				6
	MOTA	273	4 CA	LYS B 139	15.02				

-116

PCT/EP01/01457 WO 01/58951 30 ATOM

						-118				
	ATOM	2796	ND1 I	HIS B	146	13.726	46.653	18.795	1.00 53.68	7
	ATOM			HIS B		13.448	46.597	17.504	1.00 55.84	6
	ATOM	2798		HIS B		13.070	45.364	17.212	1.00 55.30	7
	ATOM	2799		HIS B		14.149	42.647	20.576	1.00 57.05	6
5	ATOM	2800		HIS B		14.640	41.984	19.644	1.00 58.04	8
-	ATOM	2801	N :	SER B	147	13.057	42.280	21.243	1.00 58.47	7
	MOTA	2802	CA	SER B	147	12.328	41.037	20.997	1.00 58.52	6
	MOTA	2803	CB	SER B	147	11.071	41.021	21.861	1.00 58.93	6
	MOTA	2804	OG	SER B	147	10.386	42.252	21.740	1.00 63.53	8
10	MOTA	2805		SER B		11.955	40.708	19.557	1.00 57.13	6 8
	MOTA	2806		SER B		11.776	39.545	19.215	1.00 56.86 1.00 56.50	7
	MOTA	2807		ARG B		11.841	41.716	18.709 17.323	1.00 58.81	6
	MOTA	2808		ARG B		11.473	41.462	16.691	1.00 62.56	6
4.5	MOTA	2809		ARG B		10.905 9.781	42.734 43.380	17.493	1.00 70.38	6
15	MOTA	2810		ARG B		9.337	44.731	16.897	1.00 76.49	6
	MOTA	2811		ARG B		8.480	45.487	17.819	1.00 82.57	7
	MOTA	2812		ARG B		7.263	45.104	18.222	1.00 84.74	6
	MOTA	2813		ARG B		6.728	43.965	17.791	1.00 85.52	7
20	MOTA	2814 2815		ARG B		6.573	45.864	19.064	1.00 85.55	7
20	MOTA	2816	C	ARG B		12.655	40.963	16.490	1.00 57.83	6
	MOTA MOTA	2817	0	ARG B		12.474	40.423	15.395	1.00 58.23	8
	MOTA	2818	N	GLU E		13.864	41.147	17.011	1.00 56.99	7
	MOTA	2819	CA	GLU E		15.072	40.743	16.306	1.00 53.60	6
25	ATOM	2820	CB	GLU E		16.015	41,933	16.216	1.00 52.91	6
	MOTA	2821	CG	GLU E		15.280	43.243	15.955	1.00 51.82	6
	MOTA	2822	CD	GLU E		16.208	44.437	15.841	1.00 54.76 1.00 55.52	6 8
	MOTA	2823	OE1	GLU E		17.132	44.562	16.672	1.00 53.32	8
	MOTA	2824	OE2	GLU E		16.010	45.261	14.929 17.036	1.00 52.75	6
30	MOTA	2825	С	GLU E		15.729	39.584	16.421	1.00 51.81	8
	MOTA	2826	0	GLU E		16.150 15.811	38.606 39.693	18.355	1.00 51.32	7
	MOTA	2827	N	ILE E		16.382	38.619	19.154	1.00 51.11	6
	MOTA	2828	CA	ILE E		17.770	38.989	19.757	1.00 48.77	6
25	MOTA	2829 2830	CB CG2			18.155	37.995	20.843	1.00 43.40	6
35	MOTA	2831		ILE I		18.842	38.967	18.672	.1.00 47.30	6
	ATOM ATOM	2832	CD1		B 150	20.219	39.315	19.168	1.00 45.12	6
	MOTA	2833	C		в 150	15.453	38.254	20.297	1.00 53.02	6
	ATOM	2834	Ö	ILE 3	в 150	14.842	39.116	20.932	1.00 52.00	8
40	ATOM	2835	N		в 151	15.350		20.539	1.00 55.16	7 6
	MOTA	2836	CA		в 151	14.542		21.628	1.00 56.52 1.00 57.06	· 6
	MOTA	2837	СВ		в 151	13.280		21.089 20.323	1.00 54.91	8
	MOTA	2838	OG		B 151	13.594		20.323	1.00 56.69	6
	MOTA	2839	C		в 151	15.452		21.685	1.00 57.55	8
45	MOTA	2840			B 151	16.144 15.480		23.661	1.00 58.35	7
	MOTA	2841	N		В 152 В 152	16.306		24.456	1.00 60.89	6
	MOTA	2842	CA CB		B 152	17.135		_	1.00 60.77	6
	MOTA MOTA	2843 2844		. VAL		17.890		24.844	1.00 59.09	6
50	ATOM	2845	CG2	VAL	в 152	16.220		26.586	1.00 62.75	6
00	ATOM	2846			в 152	15.389	33.632			6
	MOTA	2847			B 152	14.287				8
	MOTA	2848			B 153	15.845				7 6
	MOTA	2849	CA		в 153	15.028				6
55	MOTA	2850	CB		В 153	14.232				6
	MOTA	2851			B 153	13.42				8
	MOTA	2852			B 153	12.32 13.90				8
	MOTA			Z ASP	B 153 B 153	15.87				6
eΩ	MOTA			ACD	B 153	16.97			1.00 69.28	8
60	ATOM ATOM				B 154	15.40			7 1.00 70.46	7
	AIOM	2031	- ••							

PCT/EP01/01457 WO 01/58951 -119 14.409 30.740 28.876 1.00 69.92 PRO B 154 MOTA 2857 CD 16.157 29.070 28.898 1.00 72.29 PRO B 154 2858 MOTA CA 15.410 29.108 30.225 1.00 70.76 MOTA 2859 CB PRO B 154 14.902 30.494 30.281 1.00 69.28 MOTA 2860 CG PRO B 154 14.902 30.494 30.281 16.151 27.668 28.250 15.548 27.467 27.187 16.807 26.700 28.888 16.887 25.350 28.332 18.208 25.187 27.542 19.316 25.233 28.453 18.378 26.311 26.545 16.785 24.189 29.348 5 атом 1.00 75.71 2861 C PRO B 154 27.187 1.00 75.41 2862 O 2863 N 2864 CA PRO B 154 MOTA 1.00 79.33 MOTA THR B 155 1.00 83.13 THR B 155 ATOM 1.00 82.37 6 2865 CB THR B 155 MOTA 10 1.00 83.94 2866 OG1 THR B 155 MOTA 2867 CG2 THR B 155 2868 C THR B 155 2869 O THR B 155 1.00 81.49 6 MOTA 1.00 86.65 6 ATOM ATOM 7 2870 N MOTA 6 15 2871 CA MOTA 6 MOTA 2872 CB 2873 MOTA 2874 MOTA 6 MOTA 2875 C 8 20 MOTA 2876 O 7 MOTA 2877 N 6 2878 CA GLU B 157 MOTA ATOM 2879 MOTA 2880 6 25 2881 MOTA 8 MOTA 2882 8 MOTA 2883 MOTA 2884 C 2885 MOTA 7 30 MOTA 2886 6 2887 MOTA 6 2888 MOTA 2889 CG ASN B 158 6 MOTA 2890 MOTA 7 35 MOTA 2891 6 MOTA 2892 8 ATOM 2893 7 MOTA 2894 N 6 2895 MOTA 6 40 2896 MOTA 8 ATOM 2897 6 SER B 159 2898 C MOTA 1.00 87.04 8 SER B 159 MOTA 2899 O 7 ASP B 160 MOTA 2900 N б 45 ASP B 160 MOTA 2901 CA 6 CB ASP B 160 MOTA 2902 6 CG ASP B 160 2903 MOTA 8 2904 OD1 ASP B 160 MOTA OD2 ASP B 160 8 MOTA 2905 50 2906 С ASP B 160 MOTA ASP B 160 8 MOTA 2907 0 7 ASP B 161 2908 N MOTA б CA ASP B 161 MOTA 2909 6 CB ASP B 161 MOTA 2910 CG ASP B 161 55 MOTA 2911 Я OD1 ASP B 161 2912 MOTA 8 OD2 ASP B 161 MOTA 2913 1.00 69.84 21.979 39.110 6 23.957 MOTA 2914 С ASP B 161 1.00 71.09 24.569 24.527 23.008 38.843 8 ASP B 161 MOTA 2915 0 39.740 1.00 67.23 20.960 60 SER B 162 N N SER B 162 CA SER B 162 MOTA 2916 25.928 21.078 40.136 1.00 67.27 MOTA 2917

						-120				
		2010		app p 163		26.051	21.210	41.661	1.00 67.18	6
	ATOM	2918		SER B 162 SER B 162			20.020	42.315	1.00 66.16	8
	MOTA	2919 2920		SER B 162		26.787	19.922	39.653	1.00 66.71	6
	MOTA MOTA	2921		SER B 162		27.786		40.289	1.00 64.25	8
5	ATOM	2921		GLU B 163		26.410	19.330	38.523	1.00 67.10	7
3	ATOM	2923		GLU B 163		27.192	18.220	38.005	1.00 68.36	6
	ATOM	2924		GLU B 163		26.378	17.421	36.970	1.00 70.98	6
	ATOM	2925		GLU B 163		26.411	17.926	35.545	1.00 72.60	6
	ATOM	2926		GLU B 163		25.726	16.946	34.594	1.00 74.62	6
10	ATOM	2927		GLU B 163		24.477	16.828	34.649	1.00 76.45	8
	ATOM	2928		GLU B 163		26.428	16.285	33.798	1.00 74.37	8
	MOTA	2929	С	GLU B 163		28.530	18.688	37.410	1.00 67.51	6
	MOTA	2930	0	GLU B 163		29.379	17.868	37.070	1.00 67.13	8
	MOTA	2931	N	TYR B 164		28.709	20.008	37.294	1.00 66.57	7
15	MOTA	2932		TYR B 164		29.943	20.583	36.771	1.00 64.39	6
	MOTA	2933	CB	TYR B 164		29.671	21.419	35.526	1.00 64.28	6 6
	MOTA	2934	CG	TYR B 164		29.192	20.602	34.354	1.00 66.44 1.00 66.70	6
	MOTA	2935		TYR B 164		27.948	20.860	33.766 32.690	1.00 66.70	6
٠	MOTA	2936		TYR B 164		27.490	20.105	33.832	1.00 65.02	6
20	MOTA	2937		TYR B 164		29.973	19.556 18.790	32.756	1.00 65.71	6
	MOTA	2938		TYR B 164		29.524	19.075	32.730	1.00 66.77	6
	ATOM	2939	CZ	TYR B 164		28.277	18.369	31.084	1.00 67.83	8
	MOTA	2940	ОН	TYR B 164		27.819	21.463	37.826	1.00 63.28	6
	ATOM	2941	С	TYR B 164		30.584	21.936	37.662	1.00 61.67	8
25	MOTA	2942	0	TYR B 164		31.717 29.859	21.930	38.918	1.00 61.88	7
	ATOM	2943	N	PHE B 165		30.357	22.517	39.990	1.00 60.70	6
	MOTA	2944	CA	PHE B 165		29.288	22.704	41.067	1.00 58.78	6
	MOTA	2945	CB	PHE B 165		29.523	23.905	41.941	1.00 57.08	6
00	MOTA	2946	CG	PHE B 165		29.420	25.184	41,413	1.00 56.05	6
30	ATOM	2947		PHE B 165		29.888	23.757	43.272	1.00 54.09	6
	MOTA	2948		PHE B 165		29.680	26.296	42.200	1.00 55.95	6
	MOTA	2949 2950		PHE B 165		30.149	24.858	44.063	1.00 55.48	6
	MOTA	2950	CEZ	PHE B 165		30.048	26.131	43.530	1.00 56.15	6
35	MOTA	2951	C	PHE B 165		31.626	21.960	40.614	1.00 59.91	6
33	MOTA ATOM	2953	o	PHE B 16		31.757	20.760	40.808	1.00 60.17	8
	MOTA	2954	N	SER B 16		32.572	22.839	40.919	1.00 60.28	7
	ATOM	2955	CA	SER B 16		33.807	22.390	41.532	1.00 60.24	6
	MOTA	2956	СВ	SER B 16		34.810	23.534	41.647	1.00 59.33	6
40	MOTA	2957	OG	SER B 16		36.012	23.081	42.239	1.00 59.12	8
	MOTA	2958		SER B 16	6	33.468	21.877	42.916	1.00 60.82	6
	ATOM	2959		SER B 16	6	32.614	22.434	43.611	1.00 60.12	8
	MOTA	2960	N	GLN B 16		34.148	20.815	43.319	1.00 61.73	7 6
	MOTA	2961	CA	GLN B 16		33.907	20.228	44.623	1.00 62.29 1.00 63.96	6
45	MOTA	2962	CB	GLN B 16		34.228	18.737	44.576	1.00 66.77	6
	ATOM	2963		GLN B 16		35.620	18.442	44.068	1.00 68.16	6
	MOTA	2964		GLN B 16		35.827	16.969	43.736	1.00 66.24	8
	MOTA	2965		GLN B 16		35.710	16.103	44.605 42.465	1.00 68.10	7
	MOTA	2966		GLN B 16		36.136	16.682	45.689	1.00 60.72	6
50	MOTA	2967		GLN B 16		34.740	20.912	46.880	1.00 62.24	8
	MOTA	2968		GLN B 16		34.433	20.814 21.626	45.269	1.00 57.81	7
	MOTA	2969		TYR B 16		35.778		46.235	1.00 56.47	6
	ATOM	2970		TYR B 16		36.637 38.078		45.741		6
	MOTA	2973		TYR B 16		38.457		45.330		6
55	MOTA	2972		TYR B 16		38.420				6
	MOTA	297:		1 TYR B 16		38.698				6
	MOTA	297	E CE	1 TYR B 16 2 TYR B 16	, o	38.785				6
	MOTA	297	CD:	2 TYR B 16 2 TYR B 16	, o	39.060				6
60	MOTA	297		TYR B 10		39.000				6
60		297				39.270				8
	MOTA	297	ט ט	111.01		33.270				

						-121							
	» moM	2070	с т	YR B	168	36.2		23.71	12 4	46.586	1.00	55.31	6
	ATOM ATOM	2979 2980		YR B		36.8		24.39		47.356	1.00		8
	MOTA	2981		ER B		35.0		24.14		46.033	1.00		7
	ATOM	2982		ER B		34.5		25.46	69	46.299	1.00		6
5	ATOM	2983		ER B		33.3	63	25.75	55 4	45.412	1.00		6
3	MOTA	2984		ER B		32.7	75	26.99	91	45.769		55.21	8
	ATOM	2985		ER B		34.1	47	25.63	17	47.754		60.21	6
	ATOM	2986		ER B		33.6		24.6	71	48.380		62.02	8
	MOTA	2987		RG B		34.3	21	26.83	15	48.298		61.79	7
10	ATOM	2988		ARG B		33.9	38	27.0	59	49.678		60.59	6
. •	MOTA	2989		ARG B		34.4	67	28.4		50.150		61.26	6
	MOTA	2990		ARG B		35.7	81	28.3		50.904		61.61	6
	ATOM	2991		ARG B		36.5	88	29.6		50.764		66.75	6
	ATOM	2992		ARG B		35.8	66	30.8	46	51.158		69.32	7
15	ATOM	2993		ARG B	170	35.6	34	31.8	77	50.342		68.59	6
. •	MOTA	2994		ARG B		36.0)53	31.8	40	49.079		65.59	7
	ATOM	2995	NH2	ARG B	170	35.0	17	32.9		50.803		69.04	7
	ATOM	2996		ARG B		32.4		27.0		49.785		58.91	6
	ATOM	2997	0	ARG B	170	31.8		26.9		50.883		61.10	8
20	MOTA	2998		PHE B		31.7		27.0		48.650	1.00	56.02	7
	MOTA	2999	CA	PHE B	171	30.2		27.0		48.674		56.85	6
	MOTA	3000	CB	PHE B	171	29.		28.3		48.033	1.00	56.79	6 6
	ATOM	3001		PHE B		30.4		29.6		48.529	1.00	59.30	6
	ATOM	3002	CD1	PHE B	171	31.		29.8		48.110	1.00	59.59	6
25	ATOM	3003	CD2	PHE B	171	29.		30.4		49.462	1.00	58.28 58.87	6
	MOTA	3004	CE1	PHE B	171	32.		30.9		48.616	1.00	57.19	6
	MOTA	3005	CE2	PHE B		30.		31.5		49.978		58.74	6
	MOTA	3006	CZ	PHE E		31.		31.8		49.556		57.50	6
	MOTA	3007	С	PHE E		29.		25.8		47.987		57.83	8
30	MOTA	3008	0	PHE E		30.		25.0		47.439		58.25	7
	MOTA	3009	N		3 172 .		372	25.		48.036 47.416		58.95	6
	MOTA	3010	CA	GLU E			671	24.		48.436		61.94	6
	MOTA	3011	CB	GLU E			418	23.		49.634	1 00	65.83	6
	MOTA	3012	CG	GLU I			521	23.		50.637		67.36	6
35	MOTA	3013	CD	GLU I			352	21.		50.192		67.12	8
	MOTA	3014		GTM 1			275	23.		51.868		67.97	8
	ATOM	3015		GLU I			280		197	46.84		59.12	6
	MOTA	3016			B 172		369 837		217	47.30		58.48	8
	ATOM	3017			B 172		865		502	45.83		59.47	7
40	MOTA	3018		ILE :	B 173		630		911	45.18		60.85	6
	MOTA	3019			в 173 в 173		715		729	43.65	3 1.0	62.04	6
	MOTA	3020	_	ILE			. 369		077	42.99	3 1.0	0 60.25	6
	MOTA	3021		ILE	B 173		.832		603	43.08	7 1.0	0 62.02	6
ΛE	ATOM	3022 3023		TLE	B 173		.018		413	41.60		0 63.88	6
45	MOTA			TLE	B 173	_	.415	24.	148	45.66	7 1.0	0 61.72	6
	MOTA	3024 3025			B 173		.415		.919	45.73		0 61.55	8
	MOTA	3025			B 174		. 369		.883	45.99	9 1.0	0 62.91	7
	MOTA	3027			в 174		.158		.253	46.46		0 63.63	6
50	MOTA MOTA				в 174		.438		.166	47.44		0 63.66	
50	ATOM				B 174		.339		. 698	48.55	_	0 64.21	6
					B 174		.543	26	.678	49.42	8 1.0	0 63.13	6
	ATOM ATOM			LEU	в 174		.914		.532	49.36		0 61.09	6
	ATOM			LEU	в 174	20	.307	24	.010	45.23		0 64.20	6
55					в 174		.891		.885	44.96		0 65.99	
55	ATOM			ASP	в 175	20	.068	-	.058	44.45		0 64.89	7
	ATOM			ASP	в 175		.250		.895			0 66.77	
	ATOM			ASP	B 175	17	.764		.785			0 68.40) 6
	ATOM		7 CG	ASP	B 175		.806		.566			0 70.08 0 71.56	3 6 5 8
60			8 OD	1 ASP	B 175		.038		.631	41.69		00 67.36	
	ATOM			2 ASP	B 175	15	809	9 25	.322	42.40)-4 T-(,, ,,,,,	, 0

						122				
	MOM	2040	_	ASP B 175		-122 19.480	26.067	42.298	1.00 67.13	6
	ATOM ATOM	3040 3041		ASP B 175		19.400	27.160	42.703	1.00 67.04	8
	ATOM	3041		VAL B 176		19.214	25.818	41.018	1.00 66.07	7
	ATOM	3042	CA	VAL B 176		19.364	26.819	39.981	1.00 65.28	6
5	ATOM	3044	CB	VAL B 176		20.616	26.547	39.112	1.00 64.59	6
5	MOTA	3045		VAL B 176		20.681	27.529	37.943	1.00 62.08	6
	MOTA	3045		VAL B 176		21.866	26.645	39.964	1.00 64.50	6
	MOTA	3047	C	VAL B 176		18.139	26.760	39.088	1.00 66.92	6
	ATOM	3048	0	VAL B 176		17.723	25.682	38.657	1.00 68.14	8
10	ATOM	3049	N	THR B 177		17.555	27.920	38.816	1.00 68.01	7
10	ATOM	3050	CA	THR B 177		16.393	27.988	37.939	1.00 70.52	6
	ATOM	3051	СВ	THR B 177		15.087	28.139	38.744	1.00 69.59	6
	ATOM	3052	OG1	THR B 177		15.203	29.253	39.638	1.00 70.12	8
	ATOM	3053	CG2	THR B 177		14.821	26.885	39.544	1.00 68.35	6
15	MOTA	3054	С	THR B 177		16.537	29.173	36.984	1.00 72.66	6
. •	MOTA	3055	Ō	THR B 177		17.095	30.220	37.356	1.00.74.08	8
	ATOM	3056	N	GLN B 178		16.049	29.002	35.757	1.00 73.01	7
	MOTA	3057	CA	GLN B 178		16.121	30.057	34.756	1.00 74.26	6
	ATOM	3058	CB	GLN B 178		17.006	29,619	33.594	1.00 76.29	6
20	ATOM	3059	CG	GLN B 178		18.090	28.628	33.984	1.00 79.92	6
	ATOM	3060	CD	GLN B 178		19.227	28.575	32.959	1.00 83.13	6
	ATOM	3061	OE1	GLN B 178		18.993	28.495	31,731	1.00 83.91	8
	MOTA	3062	NE2	GLN B 178		20.469	28.616	33.458	1.00 82.82	7
	MOTA	3063	C	GLN B 178		14.725	30.354	34.232	1.00 73.95	6
25	MOTA	3064	0	GLN B 178		14.041	29.454	33.752	1.00 75.30	8 7
	MOTA	3065	N	LYS B 179		14.306	31.611	34.310	1.00 73.25 1.00 72.86	6
	ATOM	3066	CA	LYS B 179		12.978	31.995	33.837	1.00 72.88	6
	MOTA	3067	CB	LYS B 179		12.076	32.307	35.030	1.00 78.55	6
	ATOM	3068	CG	LYS B 179		12.196	31.282	36.160 37.428	1.00 70.33	6
30	MOTA	3069	CD	LYS B 179		11.456	31.735 30.874	38.631	1.00 80.51	6
	MOTA	3070	CE	LYS B 179		11.845	30.874	38.927	1.00 81.19	7
	MOTA	3071	NZ	LYS B 179		13.320	33.232	32.961	1.00 70.68	6
	MOTA	3072	C	LYS B 179		13.101 13.411	34.311	33.455	1.00 70.88	8
0.5	MOTA	3073	0	LYS B 179 LYS B 180		12.852	33.090	31.665	1.00 68.28	7
35	ATOM	3074	N	LYS B 180		12.970	34.242	30.776	1.00 68.69	6
	ATOM	3075 3076	CA CB	LYS B 180		12.873	33.792	29.305	1.00 66.36	6
	ATOM	3070	CG	LYS B 180		11.517	33.383	28,831	1.00 61.57	6
	MOTA ATOM	3078	CD	LYS B 180		10.763	34.578	28.296	1.00 62.84	6
40	ATOM	3079	CE	LYS B 180		11.419	35.168	27.058	1.00 63.27	6
40	ATOM	3080	NZ	LYS B 180		11.317	34.295	25.857	1.00 64.69	7
	ATOM	3081	C	LYS B 180		11.914	35.297	31.096	1.00 69.36	6
	ATOM	3082	ō	LYS B 180		11.131	35.112	32.019	1.00 70.64	8
	ATOM	3083	N	ASN B 181		11.922	36.416	30.366	1.00 69.86	7
45	ATOM	3084		ASN B 181		10.927	37.473	30.560	1.00 70.42	6
	ATOM	3085	СВ	ASN B 181		10.755	37.816	32.052	1.00 71.53	6
	MOTA	3086	CG	ASN B 181		12.058	38.021	32.760	1.00 71.03	6
	ATOM	3087		L ASN B 181		12.935	38.731	32.267	1.00 71.52	8
	ATOM	3088	ND	2 ASN B 181		12.195	37.412	33.940	1.00 71.36	7
50	MOTA	3089	С	ASN B 181		11.125	38.768	29.779	1.00 70.25	6
	MOTA	3090	0	ASN B 181		12.104	39.478	29.975	1.00 70.25	8 7
	MOTA	3091	N	SER B 182		10.162	39.078	28.911	1.00 70.77 1.00 70.64	6
	MOTA	3092				10.203	40.297	28.105		6
	MOTA	3093				9.107	40.262	27.045		8.
55	MOTA	3094				9.267	41.327	26.122 29.024		6
	MOTA	3095		SER B 182		9.997	41.500	30.095		8
	MOTA	3096		SER B 182		9.429 10.442	41.359 42.680	28.600		7
	ATOM	3097		VAL B 183 VAL B 183		10.442		29.425		6
60	MOTA	3098				11.337		30.630		6
60	MOTA	3099		1 VAL B 18		12.636		30.202		6
	MOTA	3100	,	T AWY D 10.	-					

							102				
	λ mΩM	2101	ccs	VAL B	103		-123 1.625	45.230	31.148	1.00 67.78	6
	MOTA MOTA	3101 3102		VAL B			0.590	45.189	28.659	1.00 70.59	6
	ATOM	3102		VAL B			1.522	45.282	27.853	1.00 71.25	8
	ATOM	3104	N	THR B			9.761	46.195	28.911	1.00 70.21	7
5	ATOM	3105	CA	THR B			9.949	47.480	28.250	1.00 71.59	6
J	ATOM	3106	CB	THR B			8.610	48.062	27.711	1.00 70.78	6
	ATOM	3107		THR B			8.065	47.183	26.721	1.00 69.37	8
	ATOM	3108	CG2				8.836	49.431	27.074	1.00 69.81	6
	ATOM	3109	C	THR B			0.558	48.447	29.271	1.00 73.13	6
10	ATOM	3110	Ö	THR B			0.240	48.384	30.467	1.00 73.23	8
. •	ATOM	3111	N	TYR B		1	1.449	49.319	28.806	1.00 74.37	7
	MOTA	3112	CA	TYR B		1	2.085	50.287	29.689	1.00 76.17	6
	ATOM	3113	СВ	TYR B			3.614	50.134	29.663	1.00 77.19	6
	ATOM	3114	CG	TYR B	185	1	4.076	48.723	29.912	1.00 78.36	6
15	MOTA	3115	CD1	TYR B	185	1	3.942	47.745	28.928	1.00 78.94	6
	ATOM	3116	CE1	TYR B	185	1	4.298	46.417	29.178	1.00 80.41	6
	MOTA	3117	CD2	TYR B	185	1	4.584	48.344	31.154	1.00 79.09	6
	MOTA	3118	CE2	TYR B	185	1	4.944	47.013	31.413	1.00 79.41	6
	ATOM	3119	CZ	TYR B	185		4.796	46.054	30.424	1.00 79.27	6
20	MOTA	3120	OH	TYR B			5.119	44.731	30.677	1.00 79.15	8
	MOTA	3121	C	TYR B	185		1.713	51.670	29.209	1.00 76.81	6
	ATOM	3122	0	TYR B			1.669	51.927	28.003	1.00 76.75	8
	ATOM	3123	N	SER B			.1.445	52.563	30.152	1.00 78.68	7
	MOTA	3124	CA	SER B			1.078	53.941	29.810	1.00 80.00	6
25	MOTA	3125	CB	SER B			1.002	54.795	31.089	1.00 80.19	6 8
	MOTA	3126	OG	SER B			2.160	54.610	31.902	1.00 79.86 1.00 80.21	6
	MOTA	3127	С	SER B			12.100	54.539	28.832	1.00 80.21	8
	MOTA	3128	0	SER B			11.745	55.296	27.923 29.025	1.00 79.13	7
	ATOM	3129	N	CYS B			L3.364	54.171	28.189	1.00 80.45	6
30	ATOM	3130	CA	CYS B			L4.459	54.653 54.260	26.772	1.00 81.01	6
	MOTA	3131	C	CYS B			L4.259	55.018	25.838	1.00 80.34	8
	ATOM	3132	0	CYS B			14.510	53.993	28.574	1.00 81.53	6
	MOTA	3133	CB	CYS B			15.787 15.913	52.165	28.268	1.00 84.25	16
05	MOTA	3134	SG	CYS E			13.791	53.035	26.637	1.00 82.80	7
35	MOTA	3135	N	CYS E			13.712	52.411	25.339	1.00 83.26	6
	ATOM	3136	CA	CYS E			12.352	51.851	24.849	1.00 82.46	6
	ATOM	3137 3138	C O	CYS E			11.733	50.977	25.491	1.00 82.70	8
	MOTA	3139	CB	CYS E			14.811	51.336	25.365	1.00 82.41	6
40	ATOM ATOM	3140	SG	CYS E			16.353	51.824	26.282	1.00 83.49	16
40	ATOM	3141	N	PRO E			11.891	52.346	23.679	1.00 81.48	7
	ATOM	3142	CD	PRO E			12.734	53.291	22.910	1.00 81.13	6
	ATOM	3143	CA	PRO E			10.652	52.037	22.938	1.00 79.97	6
	ATOM	3144	СВ	PRO I	3 189		10.977	52.510	21.517	1.00 80.12	6
45	ATOM	3145					11.825	53.725	21.766	1.00 80.41	6
	ATOM	3146		PRO I			10.133	50.585	22.941	1.00 78.77	6
	ATOM	3147	0	PRO I	3 189		9.063	50.303	23.490	1.00 78.66	8
	ATOM	3148	N	GLU 1	в 190		10.878	49.671	22.313	1.00 77.68	7
	ATOM	3149	CA		B 190		10.473	48.254	22.219	1.00 73.96	6
50	MOTA	3150	CB		в 190		11.214	47.570	21.075	1.00 75.24	6.
	MOTA	3151	CG		в 190		11.578		19.908	1.00 77.67 1.00 79.11	6
	MOTA	3152	CD		в 190		10.414		18.950	1.00 77.05	6 8
	MOTA	3153		1 GLU			9.731		18.617	1.00 77.05	8
	MOTA	3154		2 GLU			10.200		18.526		6
55	MOTA	3155			B 190		10.779		23.494 24.460		8
	ATOM	3156			В 190		11.317				7
	ATOM	3157			B 191		10.455				6
	ATOM	3158			B 191		10.708 9.554				6
60	MOTA	3159			В 191 В 191		12.035				6
60	MOTA	3160			B 191		12.033	_			8
	MOTA	3161	L 0	ALL	/-		,				

					_1.	24				
	лтОМ	3162	N .	TYR B 192			44.306	25.608	1.00 62.75	7
	ATOM ATOM	3163		TYR B 192			43.574	25.572	1.00 61.63	6
	ATOM	3164		TYR B 192			44.468	26.010	1.00 59.80	6
	ATOM	3165		TYR B 192	15.	.465	45.538	25.010	1.00 59.56	6
5	ATOM	3166		TYR B 192	14.	.786	46.754	25.005	1.00 59.46	6
	MOTA	3167	CE1	TYR B 192			47.728	24.036	1.00 60.27	6
	MOTA	3168	CD2	TYR B 192	16		45.315	24.027	1.00 60.64	6
	MOTA	3169	CE2	TYR B 192			46.274	23.057	1.00 60.97	6
	MOTA	3170	CZ	TYR B 192			47.480	23.064	1.00 61.60	6
10	MOTA	3171	OH	TYR B 192			48.431	22.101	1.00 60.81	8 6
	MOTA	3172	С	TYR B 192			42.302	26.426	1.00 62.58 1.00 62.03	8
	MOTA	3173	0	TYR B 192			42.349	27.668 25.738	1.00 62.66	7
	MOTA	3174	N	GLU B 193			41.166 39.852	26.384	1.00 62.77	6
4 ~	MOTA	3175	CA	GLU B 193			38.742	25.352	1.00 61.29	6
15	MOTA	3176	CB	GLU B 193			38.831	24.681	1.00 61.98	6
	MOTA	3177 3178	CG CD	GLU B 193 GLU B 193			37.636	23.775	1.00 62.41	6
	MOTA	3178		GLU B 193			36.486	24.228	1.00 62.14	8
	MOTA MOTA	3179		GLU B 193			37.838	22.621	1.00 62.38	8
20	ATOM	3181	C	GLU B 193		.105	39.552	27.091	1.00 61.37	6
20	ATOM	3182	ō	GLU B 193		.166	40.019	26.666	1.00 63.09	. 8
	ATOM	3183	N	ASP B 194	15	.026	38.772	28.165	1.00 58.46	7
	MOTA	3184	CA	ASP B 194		.207	38.395	28.914	1.00 57.68	6
	ATOM	3185	CB	ASP B 194	16	.699	39.560	29.794	1.00 58.80	6
25	MOTA	3186	CG	ASP B 194		.806	39.809	31.006	1.00 61.20	6
	MOTA	3187		ASP B 194		.115	40.864	31.030	1.00 63.41	8 8
	MOTA	3188	OD2	ASP B 194		.804	38.955	31.930	1.00 59.40	6
	MOTA	3189	C	ASP B 194		.914	37.177	29.772	1.00 56.01 1.00 55.53	8
	MOTA	3190	0	ASP B 194		.789	36.956	30.171 30.036	1.00 55.28	7
30	MOTA	3191	N	VAL B 195		.943	36.385 35.199	30.860	1.00 54.79	6
	MOTA	3192	CA	VAL B 195		3.819 7.662	34.053	30.300	1.00 53.86	6
	MOTA	3193	CB	VAL B 195		7.695	32.895	31.285	1.00 51.98	6
	MOTA	3194		VAL B 195 VAL B 195		7.112	33.631	28.968	1.00 53.24	6
25	MOTA	3195 3196	CGZ	VAL B 195		7.334	35.522	32.248	1.00 56.42	6
35	MOTA	3190	0	VAL B 195		3.451	36.003	32.407	1.00 58.47	8
	MOTA MOTA	3198	N	GLU B 196		5.525	35.261	33.261	1.00 58.06	7
	ATOM	3199	CA	GLU B 196		5.942	35,526	34.624	1.00 58.06	6
	ATOM	3200	CB	GLU B 196		5.808	36.168	35.393	1.00 59.44	6
40	ATOM	3201	CG	GLU B 196		6.168	36.535	36.811	1.00 64.02	6
, -	MOTA	3202	CD	GLU B 196		4.983	37.131	37.561	1.00 65.27	6
	MOTA	3203	OE1	L GLU B 196		4.414	38.137	37.081	1.00 65.41 1.00 68.06	8 8
	MOTA	3204	OE2			4.625	36.591	38.631	1.00 57.73	6
	MOTA	3205	С	GLU B 196		7.310	34.199 33.285	35.252 35.291	1.00 57.73	8
45	MOTA	3206				6.495		35.722	1.00 56.14	7
	MOTA	3207	N	VAL B 197		8.543 8.999	34.084 32.854	36.338	1.00 54.69	6
	MOTA	3208	CA	VAL B 19		0.358	32.405	35.757	1.00 52.53	6
	MOTA	3209	CB	VAL B 19		0.338	31.107	36.404	1.00 50.11	6
	MOTA	3210	CG.	1 VAL B 19' 2 VAL B 19'		0.241	32.229	34.264	1.00 51.73	6
50	ATOM	3211		VAL B 19		9.154	33.106	37.819	1.00 56.80	6
	MOTA	3212 3213	C	VAL B 19		9.817	34.057	38.226	1.00 57.91	8
	MOTA MOTA	3213		SER B 19		8.539	32.258	38.631	1.00 58.59	7
	MOTA	3215				8.626	32.421	40.071	1.00 58.65	6
55	ATOM	3216				7.235	32.308	40.703	1.00 59.34	6
55	MOTA	3217				6.426	33.407	40.320	1.00 59.29	8
	MOTA	3218		SER B 19	8 1	.9.556	31.385	40.651		
	MOTA	3219		SER B 19	8 1	9.340	30.188	40.505		
	ATOM	3220		LEU B 19	9 2	20.599	31.857	41.310		
60		3221		LEU B 19	9 2	21.569	30.963	41.904	_	
	ATOM	3222	CE	LEU B 19	9 2	23.000	31.437	41.622	1.00 58.76	6

						-13	25						
	ATOM	3223	CG I	EU B	199		108	30.6	670	42.358	1.00	59.80	6
	ATOM	3224		LEU B			135	29.2		41.927	1.00		6
	ATOM	3225		EU B		25	446	31.3	304	42.063	1.00		6
	MOTA	3226		LEU B			.369	30.	885	43.395	1.00		6
5	ATOM	3227	0 1	LEU B	199		.759	31.		44.136	1.00	61.67	8
	ATOM	3228	N . 2	ASN B	200		.754	29.		43.838	1.00		7
	ATOM	3229		ASN B			.539	29.		45.252	1.00	57.57 60.95	6 6
	MOTA	3230		ASN B			.188	28.		45.499		62.80	6
	MOTA	3231		ASN B			.936	28.		46.968		65.10	8
10	MOTA	3232		ASN B			.167		504	47.820 47.275	1 00	59.90	7
	MOTA	3233		ASN B			.465	28.	443	45.712	1 00	55.80	6
	MOTA	3234		ASN B			.691 .793		569	45.325	1.00	56.54	8
	MOTA	3235	_	ASN B PHE B			.561		316	46.527		53.98	7
4 =	MOTA	3236		PHE B			.725		615	47.042		53.98	6
15	MOTA	3237		PHE B			.960		975	46.226		53.35	6
	MOTA	3238 3239		PHE B			.418		404	46.418		51.26	6
	MOTA MOTA	3239		PHE B			.633		690	47.050		50.15	6
	ATOM	3241		PHE B			.615	31.	472	46.000		50.67	6
20	ATOM	3242		PHE B		27	.038	32.	015	47.264		45.58	6
	ATOM	3243		PHE B		25	.016		799	46.213		47.69	6
	ATOM	3244		PHE B		26	.227		062	46.845	1.00	46.26	6
	ATOM	3245	С	PHE B	201		.943		.080	48.456		55.95	6 8
	ATOM	3246	0	PHE B	201		.275		.017	48.912		56.39 56.81	7
25	MOTA	3247	N	ARG B			.896		.443	49.132		60.77	6
	MOTA	3248	CA	ARG E			.223		.793	50.506 51.460		64.25	6
	MOTA	3249	CB	ARG E			1.255		.104 .625	51.400	1 00	66.78	6
	MOTA	3250	CG	ARG E			1.491		.893	52.344		70.08	6
	MOTA	3251	CD	ARG E			3.494 3.768		.454	52.333		72.69	7
30	MOTA	3252	NE	ARG E			2.945		.528	52.825	1.00	73.67	6
	MOTA	3253	CZ	ARG E			1.781		.884	53.375	1.00	74.01	7
	MOTA	3254		ARG I			3.281		.245	52.760	1.00	73.29	7
	ATOM	3255	C		3 202		6.635		.328	50.843		61.67	6
35	MOTA	3256 3257		ARG I			7.181		.450	50.183		62.10	8
33	MOTA MOTA	3257			3 203		7.225		.918	51.875		62.58	7
	MOTA	3259			B 203		8.549		.505	52.298		62.87	6
	ATOM	3260			в 203	2	9.067		.417	53.399		62.83	6
	MOTA	3261			в 203	3	0.400		.995	53.967		62.29	6 6
40	ATOM	3262			B 203		0.765		.871	55.141		65.39	6
	ATOM	3263	CE		B 203		2.135		.519	55.689		70.43	7
	MOTA	3264	. NZ		B 203		3.232		772	54.695 52.854		64.30	, 6
	MOTA	3265			В 203		8.387		.101	53.371		65.43	8
	ATOM	3266			B 203		7.318		5.736 5.312	52.745		66.12	7
45	MOTA	3267			B 204		9.446		1.955	53.246	1.00	67.10	6
	MOTA	3268		LYS	B 204		0.701		1.223			63.37	6
	MOTA	3269			B 204		0.745		3.853	51.379		0 60.21	6
	MOTA	3270			B 204 B 204		1.940		2.966		1.0	0 58.61	6
EΩ	MOTA	327			B 204		1.95		2.553		1.0	0 57.79	6
50	ATOM	327			B 204		3.202		1.808		1.0	0 53.82	7
	MOTA	327 327			B 204		9.29		5.081		1.0	0 70.90	6
	MOTA	327			B 204		9.89		5.989	55.339	1.0	0 72.60	8
	MOTA	327			B 205		8.48		4.192	55.342		0 74.01	7
55	MOTA MOTA	327		GLY	B 205		28.26		4.197		_	0 74.37	6
JJ	ATOM	327			B 205		29.30	5 2	3.430		_	0 75.59	6
	MOTA				в 205	:	30.27		2.932			0 75.56	
	MOTA				в 205	:	29.16		3.331		_	0 76.47	
	MOTA						16.63		8.183			0 71.30	6
60			2 CG	PHE			17.36		9.162			0 73.66	
	MOTA			1 PHE	C 1		18.54	6 4	8.805	0.64	, 1.0	0 74.99	0
	•												

							-126				
	ATOM	3284	CD2	PHE C		L	16.889	50.471	1.160	1.00 75.46	6
	ATOM	3285		PHE C		Ĺ	19.257		-0.138	1.00 77.68	6
	ATOM	3286		PHE C		L	17.590	51.421	0.380	1.00 76.94	6
	ATOM	3287	CZ	PHE C		Ĺ	18.779	51.054	-0.271	1.00 77.37	6
5	ATOM	3288		PHE C		Ĺ	16.469	45.841	2.896	1.00 69.30	6
•	ATOM	3289		PHE C		1	15.487	45.976	3.637	1.00 68.12	8
	ATOM	3290	N	PHE C		L	15.624	46.515	0.608	1.00 67.59	7
	ATOM	3291	CA	PHE C		1	16.651	46.733	1.669	1.00 69.36	6
	ATOM	3292	N	ASP C		2	17.421	44.940	3.123	1.00 69.61	7
10	MOTA	3293	CA	ASP C		2	17.373	44.071	4.298	1.00 68.32	6
	ATOM	3294	СВ	ASP C	:	2	17.364	42.592	3.882	1.00 69.98	6
	ATOM	3295	CG	ASP C	:	2	18.729	42.092	3.426	1.00 71.56	6
	MOTA	3296	OD1	ASP C	:	2	19.586	41.867	4.316	1.00 71.73	8
	MOTA	3297	OD2	ASP C	:	2	18.936	41.926	2.187	1.00 72.36	8
15	MOTA	3298	С	ASP C	:	2	18.615	44.399	5.116	1.00 66.00	6
	ATOM	3299	0	ASP C		2	19.617	44.865	4.562	1.00 67.56	8
	ATOM	3300	N	ARG C		3	18.550	44.165	6.423	1.00 62.29	7
	MOTA	3301	CA	ARG C		3	19.663	44.455	7.320	1.00 59.37	6 6
	ATOM	3302	CB	ARG (3	19.515	43.661	8.604	1.00 56.89 1.00 55.35	6
20	MOTA	3303	CG	ARG (3	18.280	44.017	9.387	1.00 55.33	6
	MOTA	3304	CD	ARG (3	18.177	43.172	10.640	1.00 57.70	7
	MOTA	3305	NE	ARG (3	16.947	43.437 44.540	11.378 12.084	1.00 62.92	6
	MOTA	3306	CZ	ARG (3	16.714		12.166	1.00 62.52	7
	MOTA	3307		ARG (3	17.623	45.503 44.689	12.700	1.00 64.87	7
25	MOTA	3308		ARG (3	15.554 21.060	44.009	6.749	1.00 59.30	6
	ATOM	3309	C	ARG (3	21.000	45.008	7.051	1.00 61.36	8
	ATOM	3310	0	ARG (3 4	21.257	43.215	5.920	1.00 57.54	7
	ATOM	3311	N	ALA (4	22.595	43.023	5.379	1.00 55.37	6
20	ATOM	3312	CA	ALA ALA		4	22.686	41.727	4.610	1.00 53.55	6
30	ATOM	3313	CB C	ALA		4	22.947	44.186	4.478	1.00 54.97	6
	ATOM	3314 3315	0	ALA		4	24.020	44.764	4.603	1.00 55.12	8
	ATOM ATOM	3316	N	ASP		5	22.034	44.534	3.575	1.00 56.24	7
	ATOM	3317	CA	ASP		5	22.265	45.632	2.646	1.00 56.25	6
35	MOTA	3318	CB	ASP		5	21.081	45.795	1.680	1.00 58.72	6
00	MOTA	3319	CG	ASP		5	20.773	44.529	0.906	1.00 62.35	6
	ATOM	3320		ASP		5	21.715	43.900	0.364	1.00 63.21	8
	ATOM	3321		2 ASP		5	19.574	44.171	0.834	1.00 65.38	8
	ATOM	3322	С	ASP		5	22.471	46.935	3.406	1.00 55.27	6
40	MOTA	3323	0	ASP	С	5	23.294	47.764	3.020	1.00 54.31	8 7
	ATOM	3324	N	ILE	С	6	21.732	47.110	4.495	1.00 53.55	6
	ATOM	3325	CA	ILE		6	21.840	48.339	5.270	1.00 54.16 1.00 54.45	6
	ATOM	3326	CB	ILE		6	20.713	48.456	6.311	1.00 52.65	6
	MOTA	3327		2 ILE		6	20:811	49.793	7.021 5.612	1.00 56.53	6
45	MOTA	3328		1 ILE		6	19.352	48.344 48.530	6.524	1.00 56.74	6
	MOTA	3329		1 ILE		6	18.146	48.475	5.972	1.00 52.95	6
	MOTA	3330		ILE		6	23.178 23.872	49.487	5.818	1.00 53.74	8
	MOTA	3331		ILE		6	23.543	47.455	6.741	1.00 51.30	7
	MOTA	3332		LEU		7 7	24.814		7.460	1.00 49.62	6
50	MOTA	3333				7	24.931		8.293	1.00 47.45	6
	MOTA	3334				7	23.912		9.429	1.00 47.62	6
	ATOM	3335		1 LEU		7	.23.819		10.014		6
	ATOM	3336 3337		2 LEU		7	24.321		10.486		6
55	ATOM ATOM	3338		LEU		7	25.970		6.465		6
55		3339		LEU		7	26.951		6.677	1.00 47.57	8
	MOTA MOTA			TYR		8	25.827		5.361	1.00 52.00	7
	MOTA					8	26.830				6
	MOTA					8	26.367	45.961	_		6
60	MOTA					8	27.335			1.00 57.66	6
	ATOM			1 TYR	C	8	28.552	45.289	2.106	1.00 58.72	6

	W O 01/30	<i>) 1</i>							101/2101/01	•
						-127				
	ATOM	3345	CE1	TYR C	8	29.467	45.315	1.045	1.00 60.33	6
	ATOM	3345		TYR C	8	27.051	46.679	0.851	1.00 58.73	6
				TYR C	8	27.957	46.714	-0.211	1.00 60.05	6
	ATOM	3347				29.162	46.027	-0.107	1.00 60.68	6
_	MOTA	3348		TYR C	8		46.045	-1.163	1.00 62.86	8
5	MOTA	3349		TYR C	8	30.045		3.790	1.00 54.25	6
	MOTA	3350	С	TYR C	8	27.134	48.235		1.00 54.25	8
	MOTA	3351	0	TYR C	8	28.298	48.589	3.614		
	MOTA	3352	N	ASN C	9	26.092	49.015	3.516	1.00 53.76	7
	MOTA	3353	CA	ASN C	9	26.283	50.369	3.013	1.00 55.35	6
10	MOTA	3354	CB	ASN C	9	24.941	51.005	2.660	1.00 59.27	6
	ATOM	3355	CG	ASN C	9	24.299	50.372	1.433	1.00 61.31	6
	MOTA	3356		ASN C	9	24.907	49.531	0.758	1.00 61.18	8
	MOTA	3357		ASN C	9	23.068	50.778	1.136	1.00 62.69	7
	ATOM	3358	C	ASN C	9	27.003	51.233	4.034	1.00 54.14	6
15		3359	0	ASN C	9	28.001	51.877	3.722	1.00 54.09	8
13	MOTA			ILE C	10	26.494	51.240	5.258	1.00 54.05	7
	MOTA	3360	N		10	27.107	52.014	6.330	1.00 54.35	6
	MOTA	3361	CA	ILE C		26.399	51.757	7.668	1.00 53.88	6
	MOTA	3362	CB	ILE C	10		52.453	8.784	1.00 52.27	6
	MOTA	3363		ILE C	10	27.141		7.595	1.00 53.43	6
20	MOTA	3364		ILE C	10	24.956	52.257		1.00 51.08	6
	MOTA	3365	CD1	ILE C	10	24.114	51.860	8.769		6
	ATOM	3366	C	ILE C	10	28.580	51.635	6.479	1.00 55.70	
	MOTA	3367	0	ILE C	10	29.452	52.497	6.609	1.00 56.88	8
	ATOM	3368	N	ARG C	11	28.844	50.337	6.456	1.00 56.11	7
25	ATOM	3369	CA	ARG C	11	30.194	49.827	6.579	1.00 57.74	6
	MOTA	3370	CB	ARG C	11	30.161	48.307	6.466	1.00 61.80	6
	ATOM	3371	CG	ARG C	11	31.495	47.629	6.644	1.00 67.28	6
		3372	CD	ARG C	11	31.879	47.631	8.102	1.00 75.61	6
	MOTA		NE	ARG C	11	32.848	46.586	8.419	1.00 82.91	7
00	MOTA	3373		ARG C	11	32.779	45.333	7.957	1.00 86.49	6
30	MOTA	3374	CZ			31.785	44.963	7.140	1.00 87.62	7
	ATOM	3375		ARG C	11	33.689	44.436	8.331	1.00 87.96	7
	MOTA	3376		ARG C	11			5.490	1.00 57.06	6
	MOTA	3377	С	ARG C	11	31.099	50.388	5.758	1.00 57.56	8
	MOTA	3378	0	ARG C	11	32.198	50.865		1.00 57.22	7
35	MOTA	3379	N	GLN C	12	30.617	50.333	4.255	1.00 57.22	6
	MOTA	3380	CA	GLN C	12	31.377	50.781	3.093		6
	MOTA	3381	CB	GLN C	12	30.783	50.169	1.829	1.00 56.62	
	ATOM	3382	CG	GLN C	12	31.795	49.448	0.976	1.00 58.01	6
	MOTA	3383		GLN C	12	32.113	48.101	1.532	1.00 58.10	6
40	ATOM	3384		1 GLN C	12	31.215	47.289	1.704	1.00 59.91	8
40	MOTA	3385		2 GLN C	12	33.384	47.846	1.824	1.00 57.19	7
		3386		GLN C	12	31.505	52.278	2.872	1.00 56.02	6
	MOTA			GLN C	12	32.424	52.728	2.208	1.00 54.27	8
	MOTA	3387		THR C	13	30.589	53.054	3.423	1.00 58.04	7
4-	MOTA	3388				30.631	54.492	3.213	1.00 59.72	6
45	MOTA	3389				29.302		2.653	1.00 58.83	6
	MOTA	3390) CB		13			3.559	1.00 55.46	8
	ATOM	3391	L OG	1 THR C		28.253			1.00 59.29	6
	MOTA	3392	CG			29.043		1.277	1.00 55.25	6
	ATOM	3393	3 C	THR C	13	30.944		4.459		
50		3394	1 0	THR C	13	31.317		4.364		8
	ATOM	3395		SER C	14	30.794	54.705	5.627	1.00 62.55	7
	MOTA	3396		_		31.053	55.421	6.865		6
		3391				30.549	54.612	8.056		6
	MOTA			_		30.476		9.209	1.00 64.16	8
	MOTA	3398				32.521		7.074		6
55		339		SER C		33.422		6.577		8
	MOTA	340		SER C		32.735				7
	MOTA			ARG C						6
	MOTA					34.064				6
	MOTA	340	3 CE			34.383				6
60	MOTA	340	4 C			34.388				6
	ATOM	340	5 CI) ARG (15	35.114	4 59.331	4.968	1.00 01.90	U

						-128			•	
	ATOM	3406	NE	ARG C	15	36.475	59.479	5.475	1.00 64.09	7
	MOTA	3407		ARG C	15	37.287	60.488	5.180	1.00 63.60	6
	MOTA	3408		ARG C	15	36.873	61.450	4.375	1.00 62.16	7
	MOTA	3409	NH2	ARG C	15	38.516	60.526	5.688	1.00 66.26	7
5	MOTA	3410	С	ARG C	15	34.081	57.753	9.598	1.00 54.80	6
	MOTA	3411	0	ARG C	15	33.736	58.874	9.969	1.00 54.31	8
	MOTA	3412	N	PRO C	16	34.483	56.811	10.460	1.00 53.16	7
	MOTA	3413	CD	PRO C	16	34.921	55.451	10.106	1.00 49.32	6 6
4.0	MOTA	3414	CA	PRO C	16	34.547	57.012	11.911	1.00 51.93 1.00 49.26	6
10	MOTA	3415	CB	PRO C	16	35.072	55.668	12.429 11.387	1.00 49.20	6
	MOTA	3416	CG	PRO C	16	34.647	54.702 58.172	12.356	1.00 51.62	6
	MOTA	3417	C	PRO C	16	35.420 35.266	58.663	13.468	1.00 52.27	8
	MOTA	3418	0	PRO C	16 17	36.337	58.608	11.501	1.00 51.78	7
15	MOTA	3419	N	ASP C	17	37.219	59.706	11.863	1.00 54.16	6
15	MOTA	3420 3421	CA CB	ASP C	17	38.597	59.526	11.209	1.00 59.36	6
	MOTA MOTA	3421	CG	ASP C	17	39.421	58.411	11.859	1.00 64.02	6
	ATOM	3423		ASP C	17	39.200	58.134	13.067	1.00 64.61	8
	ATOM	3424		ASP C	17	40.299	57.824	11.170	1.00 64.76	8
20	ATOM	3425	C	ASP C	17	36.680	61.080	11.499	1.00 53.77	6
	ATOM	3426	ō	ASP C	17	37.350	62.088	11.736	1.00 54.82	8
	ATOM	3427	N	VAL C	18	35.473	61.129	10.944	1.00 53.02	7
	MOTA	3428	CA	VAL C	18	34.902	62.398	10.528	1.00 53.40	6
	ATOM	3429	CB	VAL C	18	34.699	62.421	9.003	1.00 53.89	6
25	MOTA	3430	CG1	VAL C	18	34.194	63.785	8.563	1.00 53.62	6
	MOTA	3431	CG2	VAL C	18	36.013	62.087	8.308	1.00 52.31	6
	MOTA	3432	С	VAL C	18	33.589	62.771	11.201	1.00 54.75 1.00 54.30	6 8
	MOTA	3433	0	VAL C	18	32.573	62.097	11.046	1.00 54.30	7
	MOTA	3434	N	ILE C	19	33.634	63.870	11.944 12.662	1.00 55.34	6
30	MOTA	3435	CA	ILE C		32.480	64.401 65.631	13.519	1.00 54.46	6
	MOTA	3436	CB	ILE C	19	32.934 33.362	66.777	12.618	1.00 53.28	6
	ATOM	3437		ILE C		31.827	66.078	14.467	1.00 53.52	6
	MOTA	3438		. ILE C		32.318	67.022	15.525	1.00 50.20	6
35	MOTA	3439	CDI	ILE C		31.392	64.784	11.644	1.00 56.25	6
33	MOTA MOTA	3440 3441	0	ILE C		31.675	65.474	10.653	1.00 56.64	8
	ATOM	3442	N	PRO C		30.142	64.318	11.861	1.00 55.95	7
	MOTA	3443	CD	PRO C		29.756	63.451	12.978	1.00 55.72	6
	ATOM	3444	CA	PRO C		28.980	64.574	10.996	1.00 57.07	6
40	ATOM	3445		PRO C		27.912	63.627	11.540	1.00 55.92	6
	ATOM	3446	CG	PRO C	20	28.673	62.639	12.349	1.00 57.30	6
	MOTA	3447	С	PRO C	20	28.500	66.023	11.035	1.00 59.85	6
	MOTA	3448	0	PRO C	20	27.326		11.270	1.00 58.63	8 7
	MOTA	3449	N	THR C		29.416		10.782	1.00 64.15 1.00 68.52	6
45	MOTA	3450		THR C		29.123	68.370	10.797	1.00 68.32	6
	MOTA	3451	CB	THR C		30.421		11.046	1.00 08.47	8
	MOTA	3452		1 THR C		30.496		12.440 10.216	1.00 69.90	6
	MOTA	3453				30.470		9.555	1.00 72.31	6
	MOTA	3454		THR C		28.424 28.826		8,412	1.00 71.25	8
50	MOTA	3455		THR C		27.384		9.805	1.00 76.61	7
	MOTA	3456		GLN (26.599		8,747	1.00 80.67	6
	MOTA	3457 3458				25.112		8.972	1.00 81.49	6
	MOTA	3459				24.749		9.029	1.00 82.93	6
55	MOTA MOTA	3450				23.534			1.00 83.25	6
55	ATOM	3461		1 GLN		23.566		11.120	1.00 84.14	8
	MOTA					22.452	67.867	9.285		7
	MOTA	3463		GLN (26.865			1.00 83.04	6
	MOTA			GLN		26.382				8
60	ATOM			ARG	C 23	27.635				7
	MOTA		6 CA	ARG	C 23	27.985	73.783	7.802	1.00 86.39	6

						-129				_
	MOTA	3467	CB .	ARG C	23		74.654	7.771	1.00 87.20	6
	MOTA	3468	CG .	ARG C	23	26.050	74.710	6.393	1.00 89.96	6
	ATOM	3469	CD .	ARG C	23	24.797	73.834	6.297	1.00 90.96	6
	ATOM	3470		ARG C	23	24.282	73.771	4.920	1.00 93.30	7
5	ATOM	3471		ARG C	23	23.996	74.830	4.145	1.00 94.77	6
•	ATOM	3472	_	ARG C	23	24.167	76.083	4.591	1.00 94.25	7
	MOTA	3473		ARG C	23	23.537	74.640	2.905	1.00 94.32	7
	ATOM	3474		ARG C	23	28.828	74.134	9.013	1.00 85.61	6
	ATOM	3475		ARG C	23	29.599	73.302	9.495	1.00 85.98	8
10	MOTA	3476	-	ASP C	24	28.700	75.358	9.503	1.00 85.83	7
10	ATOM	3477		ASP C	24	29.462	75.755	10.685	1.00 86.66	6
	ATOM	3478		ASP C	24	29.625	77.283	10.785	1.00 90.61	6
	ATOM	3479	CG	ASP C	24	29.385	78.002	9.458	1.00 92.74	6
	ATOM	3480		ASP C	24	30,108	77.704	8.471	1.00 93.41	8
15	ATOM	3481		ASP C	24	28.468	78.868	9.418	1.00 93.68	8
10	ATOM	3482	C	ASP C	24	28.679	75.280	11.907	1.00 85.20	6
	MOTA	3483	0	ASP C	24	29.053	75.591	13.052	1.00 85.29	8
	ATOM	3484	N	ARG C	25	27.587	74.553	11.660	1.00 82.29	7
	ATOM	3485	CA	ARG C	25	26.761	74.039	12.742	1.00 79.75	6
20	ATOM	3486	CB	ARG C	25	25.422	73.522	12.210	1.00 82.55	6
20	ATOM	3487	CG	ARG C	25	24.428	74.588	11.781	1.00 86.91	6
	MOTA	3488	CD	ARG C	25	23.026	73.964	11.594	1.00 91.01	6
	MOTA	3489	NE	ARG C	25	22.007	74.963	11.252	1.00 94.97	7
		3490	CZ	ARG C	25	20.702	74.705	11.146	1.00 96.54	6
25	ATOM ATOM	3491		ARG C	25	20.253	73.471	11.356	1.00 97.65	7
20	ATOM	3492		ARG C	25	19.844	75.679	10.837	1.00 96.40	7
	ATOM	3493	C	ARG C	25	27.456	72.906	13.490	1.00 76.53	6
	ATOM	3494	Ö	ARG C	25	28.004	71.987	12.876	1.00 78.25	8
		3495	N	PRO C	26	27.449	72.963	14.829	1.00 72.39	7
30	ATOM	3496	CD	PRO C	26	27.074	74.126	15.647	1.00 71.70	6
30	MOTA	3497	CA	PRO C	26	28.073	71.935	15.660	1.00 68.13	6
	MOTA	3498	CB	PRO C	26	28.087	72.574	17.050	1.00 69.12	6
	MOTA	3499	CG	PRO C	26	28.066	74.039	16.770	1.00 69.98	6
	MOTA		C	PRO C	26	27.183	70.706	15.639	1.00 64.71	6
25	MOTA	3500 3501	0	PRO C	26	26.010	70.795	15.275	1.00 63.13	8
35	MOTA	3501	N	VAL C	27	27.735	69.560	16.019	1.00 61.55	7
	MOTA		CA	VAL C	27	26.937	68.349	16.081	1.00 57.92	6
	MOTA	3503 3504	CB	VAL C	27	27.805	67.073	15.948	1.00 56.85	6
	MOTA	3504		VAL C	27	27.038	65.860	16.439	1.00 54.71	6
40	MOTA	3505		VAL C	27	28.197	66.872	14.502	1.00 54.24	6
40	MOTA	3507	C	VAL C	27	26.301	68.400	17.452	1.00 56.84	6
	ATOM	3508	Ö	VAL C		26.987	68.621	18.450	1.00 57.02	8
	ATOM ATOM	3509	И	ALA C	28	24.989	68.228	17.506	1.00 56.11	7
	ATOM	3510	CA	ALA C		24.302	68.262	18.783	1.00 54.82	6
45		3511		ALA C	_	22.896	68.775	18.600	1.00 55.72	6
40	MOTA MOTA	3512	c	ALA C		24.282	66.879	19.424	1.00 54.45	6
		3512		ALA C	_	23.579	65.972	18.964	1.00 54.53	8
	MOTA	3514		VAL C		25.067	66.742	20.488	1.00 53.25	7
	ATOM	3515		VAL C		25.191	65.503	21.235	1.00 51.65	6
50	MOTA	3516		VAL C		26.676	65.113	21.450	1.00 50.25	6
50	MOTA	3517		1 VAL C		26.770	63.846	22.297	1.00 47.03	6
	MOTA	3518		2 VAL C		27.358	64.921	20.108	1.00 50.21	6
	MOTA	3519		VAL		24.549	65.670	22.595	1.00 52.02	6
	ATOM	3520		VAL		24 833	66.615	23.320	1.00 51.40	8
55	MOTA	3521		SER C		23.669	64.745	22.932		7
55	ATOM	3522		SER C		23.012		24.214	1.00 55.39	6
	MOTA MOTA	3523				21.495		24.034	1.00 54.53	6
						21.159		23.373		8
	MOTA MOTA			SER (23.566		25.013		6
60				SER (23.688		24.503		8
	MOTA			VAL		23.916		26.261	1.00 56.76	7
	11 OF	552								

	WO 01/58	951					•		PCT/EP01/014	157
	., 0 01,00					-130				
	MOTA	3528	CA \	AL C	31	24.466	62.893	27.174	1.00 57.06	6
	ATOM	3529	_	AL C	31	25.871	63.301	27.640	1.00 57.34	6
	ATOM	3530	CG1 V		31	26.543	62.141	28.354	1.00 57.65	6
	MOTA	3531	CG2 V		31	26.674		26.467	1.00 58.89	6
5	MOTA	3532		/AL C	31	23.585		28.415	1.00 57.25	6
9	MOTA	3533		/AL C	31	23.152		28.979	1.00 57.25	8
		3534		SER C	32	23.339		28.855	1.00 56.49	7
	MOTA	3535		SER C	32	22.505		30.024	1.00.57.63	6
	MOTA	3536		SER C	32	21.045		29.589	1.00 59.80	6
10	MOTA	3537		SER C	32	20.220		30.667	1.00 63.17	8
10	MOTA			SER C	32	22.958		30.781	1.00 57.81	6
	ATOM	3538		SER C	32	22.860		30.271	1.00 60.21	8
	MOTA	3539		LEU C	33	23.448		31.997	1.00 56.08	7
	MOTA	3540			33	23.895		32.801	1.00 55.73	6
4-	ATOM	3541		LEU C	33	25.021		33.752	1.00 53.14	6
15	MOTA	3542	_	LEU C		26.240		33.105	1.00 52.98	6
	MOTA	3543		LEU C	33	27.353		34.127	1.00 51.17	6
	ATOM	3544		LEU C	33	26.680		31.933	1.00 53.34	6
	ATOM	3545		LEU C	33	22.752		33.624	1.00 56.29	6
	ATOM	3546		LEU C	33			34,193	1.00 57.63	8
20	ATOM	3547		LEU C	33	21.976		33.664	1.00 54.96	7
	MOTA	3548		LYS C	34	22.642		34.447	1.00 55.26	6
	MOTA	3549		LYS C	34	21.616		33.563	1.00 58.99	6
	MOTA	3550		LYS C	34	20.71		32.414	1.00 63.56	6
	MOTA	3551		LYS C	34	20.05		32.414	1.00 68.99	6
25	MOTA	3552	_	LYS C	34	19.09	•	31.705	1.00 71.13	· 6
	MOTA	3553	CE	LYS C	34	18.49		32.120	1.00 71.58	7
	ATOM	3554	NZ	LYS C	34	17.52	_	35.369	1.00 71.30	6
	ATOM	3555	С	LYS C	34	22.41			1.00 54.63	8
	MOTA	3556	0	LYS C	34	23.03		34.922	1.00 54.05	7
30	MOTA	3557	N	PHE C	35	22.41		36.657	1.00 53.24	6
	MOTA	3558	CA	PHE C	35	23.19		37.579	1.00 31.20	6
	MOTA	3559	CB	PHE C	35	23.42		38.864	1.00 48.89	6
	MOTA	3560	CG	PHE C	35	24.29		38.662	1.00 48.34	6
	ATOM	3561		PHE C	35	23.74		38.239	1.00 50.53	6
35	MOTA	3562		PHE C	35	25.66		38.814	1.00 47.39	6
	MOTA	3563		PHE C	35	24.55			1.00 47.33	6
	ATOM	3564	CE2	PHE C	35	26.48			1.00 30.73	6
	MOTA	3565	CZ	PHE C	35	25.92			1.00 50.23	6
	MOTA	3566	С	PHE C	35	22.60			1.00 50.29	8
40	MOTA	3567	0	PHE C	35	21.41			1.00 49.55	7
	MOTA	3568	N	ILE C	36	23.47			1.00 47.28	6
	MOTA	3569	CA	ILE C	36	23.09			1.00 46.86	6
	MOTA	3570	CB	ILE C	36	23.65			1.00 44.45	6
	MOTA	3571		ILE C	36	23.17	-		1.00 46.79	6
45	MOTA	3572		ILE C	36	23.25			1.00 48.67	6
•	MOTA	3573	CD1	ILE C	36	21.75			1.00 46.88	6
	MOTA	3574	С	ILE C	36	23.61				8
	MOTA	3575	0	ILE C	36	23.05				7
	MOTA	3576	N	ASN C		24.71				6
50	MOTA	3577	CA	ASN C	37	25.27				6
	MOTA	3578	CB	ASN C		25.73				6
•	ATOM	3579	CG	ASN C		25.68				
	ATOM	3580		ASN C		26.0				8 7
	MOTA	3581	ND2	ASN C	37	25.20				
55		3582		ASN C		26.43				6
	MOTA	3583		ASN C	37	27.0				8
	ATOM	3584		ILE C	38	26.6				7
	MOTA	3585		ILE C	38	27.7				6
	MOTA	3586	СВ	ILE C		27.1				6
60		3587	CG2	ILE C		28.3				6
	MOTA			LILE	38	26.4	18 54.77	0 43.584	1 1.00 42.70	6

	WO 01/58	951					121			PCT/EP01/0145	57
	ATOM	3589	CD1	ILE C	38		-131 25 <i>.</i> 630	55.758	44.343	1.00 40.81	6
	MOTA	3590	С	ILE C	38		28.432	51.585	44.306	1.00 49.67	6 8
	MOTA	3591	0	ILE C	38		27.890	51.083	45.281	1.00 53.17 1.00 51.33	7
_	MOTA	3592		LEU C	39		29.636	51.228	43.872 44.468	1.00 51.33	6
5	ATOM	3593		LEU C	39		30.378 31.113	50.125 49.384	43.353	1.00 53.88	6
	MOTA	3594	CB	LEU C	39 39		30.167	49.000	42.215	1.00 55.35	6
	ATOM	3595 3596	CG CD1	LEU C	39		30.932	48.308	41.115	1.00 54.78	6
	MOTA MOTA	3597		LEU C	39		29.053	48.097	42.760	1.00 54.41	6
10	ATOM	3598	C	LEU C	39		31.334	50.367	45.619	1.00 53.89	6
. •	ATOM	3599	Ō	LEU C	39		31.386	49.567	46.558	1.00 53.73	8
	ATOM	3600	N	GLU C	40		32.124	51.426	45.536	1.00 54.34	7
	MOTA	3601	CA	GLU C	40		33.058	51.714	46.602	1.00 56.97	6
	MOTA	3602	CB	GTA C	40		34.446	51.211	46.271	1.00 59.79	6 6
15	MOTA	3603	CG	GLU C	40		34.555	49.711	46.147	1.00 67.48 1.00 70.43	6
	MOTA	3604	CD	GLU C			35.996	49.266	45.979 44.998	1.00 70.43	8
	MOTA	3605		GLU C			36.647 36.471	49.719 48.476	46.832	1.00 71.19	8
	MOTA	3606	_	GLU C			33.125	53.192	46.823	1.00 57.35	6
00	ATOM	3607	C	GLU C			33.123	53.132	45.886	1.00 58.85	8
20	ATOM	3608	O N	VAL C			33.132	53.572	48.084	1.00 57.50	7
	ATOM ATOM	3609 3610	CA	VAL C			33.202	54.964	48.440	1.00 56.50	6
	ATOM	3611	CB	VAL C			31.845	55.447	49.000	1.00 57.37	6
	ATOM	3612		VAL C			31.972	56.832	49.567	1.00 56.32	6
25	ATOM	3613		VAL C			30.797	55.437	47.894	1.00 57.94	6
	ATOM	3614	С	VAL C	41		34.289	55.098	49.486	1.00 55.27	6
	MOTA	3615	0	VAL C			34.502	54.200	50.300	1.00 54.09 1.00 55.74	8 7
	MOTA	3616	N	ASN C			34.994	56.216	49.433	1.00 55.74	6
	MOTA	3617	CA	ASN C	_		36.053	56.504	50.379 49.787	1.00 53.03	6
30	MOTA	3618	СВ	ASN (37.418	56.169 56.155	50.833	1.00 53.86	6
	MOTA	3619	CG	ASN (38.509 38.622	57.075	51.634	1.00 54.42	8
	ATOM	3620		ASN (39.325	55.110	50.828	1.00 54.04	7
	ATOM	3621 3622	C MD2	ASN (35.947	57.994	50.635	1.00 58.42	6
35	MOTA MOTA	3623	Ö	ASN (36.322	58.806	49.786	1.00 58.83	8
00	ATOM	3624	N	GLU (35.408	58.348	51.801	1.00 60.55	7
	ATOM	3625	CA	GLU	C 4:	3	35.242	59.744	52.163	1.00 61.17	6
	ATOM	3626	CB	GLU (C 4:	3	34.269	59.874	53.327	1.00 63.37	6 6
	MOTA	3627	CG	GLU			33.932	61.318	53.646	1.00 67.39 1.00 68.69	6
40	MOTA	3628	CD	GLU			32.773	61.463	54.616	1.00 69.27	8
	MOTA	3629					32.494	62.613 60.444	55.019 54.964	1.00 68.84	8
	MOTA	3630					32.142 36.571	60.391	52.524	1.00 60.37	6
	ATOM	3631	_	GLU			36.706				8
15	MOTA	3632		GLU ILE			37.544	59.567	52.903	1.00 59.67	7
45	ATOM ATOM	3633 3634					38.874	60.051	53.254	1.00 60.12	6
	ATOM	3635					39.727	58.944	53.908	1.00 60.72	6
	ATOM	3636		2 ILE			41.124	59.469	54.194	1.00 61.61	6
	ATOM	3637		1 ILE		4	39.081	58.470	55.206	1.00 62.18	6
50		3638		1 ILE		4	39.142	59.479			6
	MOTA	3639) C	ILE		4	39.617	60.514			6 8
	MOTA	3640	0	ILE		4	40.255				7
	MOTA	3641		THR		5	39.540				6
	MOTA	3642				5	40.221				6
55		3643				5	39.776				8
	MOTA	3644		1 THR		.5 .5	41.812				6
	MOTA	3649		2 THR THR		:5 !5	39.325				6
	MOTA	3640 3641		THR		.5	39.801				8
60	MOTA (ASN		16	38.029			1.00 51.51	7
30	ATOM					6	37.106		48.002	1.00 52.39	6

	• • • • • • • • • • • • • • • • • •									
						-132	co o c	47 000	1 00 54 02	6 ·
	MOTA	3650		ASN C	46	37.420	62.856	47.890	1.00 54.02	6
	ATOM	3651	CG	ASN C	46	36.525	63.703	48.766	1.00 56.29	
	ATOM	3652	OD1	ASN C	46	36.877	64.821	49.132	1.00 59.35	8
	MOTA	3653	ND2	ASN C	46	35.357	63.182	49.093	1.00 53.30	7
5	ATOM	3654	С	ASN C	46	37.143	60.711	46.618	1.00 52.56	6
	ATOM	3655		ASN C	46	37.269	61.376	45.587	1.00 51.60	8
	MOTA	3656	N	GLU C	47	37.013	59.392	46.610	1.00 51.63	7
	MOTA	3657	CA	GLU C	47	37.023	58.633	45.376	1.00 50.56	6
	MOTA	3658	CB	GLU C	47	38.307	57.805	45.300	1.00 49.50	6
10	ATOM	3659	CG	GLU C	47	39.566	58.650	45.210	1.00 49.79	6
	ATOM	3660	CD	GLU C	47	40.823	57.810	45.227	1.00 51.38	6
	ATOM	3661	OE1	GLU C	47	40.741	56.621	44.860	1.00 52.93	8
	ATOM	3662	OE2	GLU C	47	41.892	58.339	45.595	1.00 51.30	8
	MOTA	3663	C	GLU C	47	35.793	57.734	45.314	1.00 48.78	6
15	MOTA	3664	ō	GLU C	47	35.403	57.133	46.300	1.00 48.46	8
	MOTA	3665	N	VAL C	48	35.178	57.654	44.147	1.00 47.95	7
	MOTA	3666	CA	VAL C	48	33.998	56.834	43.993	1.00 49.71	6
	ATOM	3667	CB	VAL C	48	32.768	57.701	43.736	1.00 50.43	6
	MOTA	3668		VAL C	48	31.549	56.834	43.578	1.00 53.94	6
20	MOTA	3669		VAL C	48	32.567	58.645	44.869	1.00 52.35	6
20	MOTA	3670	C	VAL C	48	34.130	55.838	42.850	1.00 49.77	6
	ATOM	3671	Ö	VAL C	48	34.686	56.146	41.802	1.00 49.93	8
	ATOM	3672	N	ASP C	49	33.615	54.636	43.068	1.00 49.86	7
	ATOM	3673	CA	ASP C	49	33.646	53.595	42.061	1.00 49.59	6
25	ATOM	3674	СВ	ASP C	49	34.261	52.331	42.644	1.00 51.71	6
20	ATOM	3675	CG	ASP C	49	34.714	51.366	41.580	1.00 51.64	6
	ATOM	3676		ASP C	49	33.992	51.233	40.581	1.00 50.25	8
	ATOM	3677		ASP C	49	35.777	50.736	41.748	1.00 51.89	8
	MOTA	3678	C	ASP C	49	32.181	53.382	41.728	1.00 49.00	6
30	ATOM	3679	Ö	ASP C	49	31.437	52.818	42.524	1.00 51.14	8
50	MOTA	3680	N	VAL C	50	31.770	53.840	40.551	1.00 48.30	7
	ATOM	3681	CA	VAL C	50	30.374	53.757	40.147	1.00 48.89	6
	MOTA	3682	СВ	VAL C	50	29.755	55.185	40.167	1.00 51.49	6
	ATOM	3683		VAL C	50	30.212	55.964	38.944	1.00 50.49	6
35	MOTA	3684		VAL C	50	28.248	55.120	40.223	1.00 53.32	6
00	ATOM	3685	C	VAL C	50	30.130	53.122	38.771	1.00 47.56	6
	ATOM	3686	Ö	VAL C		31.012	53.080	37.928	1.00 49.11	8
	MOTA	3687	N	VAL C		28.917	52.621	38.574	1.00 44.81	7
	MOTA	3688	CA	VAL C		28.484	52.003	37.324	1.00 43.09	6
40	ATOM	3689	СВ	VAL C	_	28.003	50.542	37.539	1.00 41.28	· 6
-10	ATOM	3690		L VAL C		27.355	50.017	36.267	1.00 37.45	6
	ATOM	3691		VAL C		29.157	49.659	37.953	1.00 36.77	6
	ATOM	3692	C	VAL C		27.300	52.817	36.781	1.00 44.98	6
	ATOM	3693	0	VAL C		26.385	53.163	37.522	1.00 46.72	8
45	ATOM	3694		PHE C		27.299	53.113	35.490	1.00 44.48	7
	ATOM	3695		PHE C	52	26.206	53.883	34.937	1.00 45.00	6
	MOTA	3696		_		26.469	55.352	35.210		6
	ATOM	3697				27.729	55.857			6
	ATOM	3698		1 PHE		27.735	56.327			6
50	ATOM	3699		2 PHE		28.921	55.841			6
-	MOTA	3700		1 PHE		28.908	56.771			6
	ATOM	3701		2 PHE		30.102				6
	ATOM	. 3702				30.098				6
	ATOM	3703		PHE (26.048				6
55	ATOM	3704		PHE (26.932				8
•	MOTA	3705		TRP		24.918				7
	ATOM					24.684				6
	ATOM					23.251				6
	MOTA		G CG	TRP		22.915				6
60			CE	2 TRP		21.615				6
	MOTA			2 TRP	C 53	21.748	50.311	32.002	1.00 49.66	6

						-133				
	MOTA	3711	CE3	TRP C	53	20.342	52.106	31.170	1.00 51.64	6
	ATOM	3712	CD1	TRP C	53	23.765	51.259	32.008	1.00 48.94	6
	MOTA	3713		TRP C	53	23.073	50.107	32.284	1.00 48.58	7
	MOTA	3714	CZ2	TRP C	53	20.659	49.448	32.120	1.00 50.24	6
5	MOTA	3715	CZ3	TRP C	53	19.258	51.250	31.286	1.00 51.60	6
	MOTA	3716	CH2	TRP C	53	19.424	49.935	31.759	1.00 52.14	6
	MOTA	3717	С	TRP C	53	24.940	55.339	30.862	1.00 48.39	6
	ATOM	3718	0	TRP C	53	24.234	56.290	31.156	1.00 50.70	8
	MOTA	3719	И	GLN C	54	25.946	55.429	30.010	1.00 49.71	7
10	MOTA	3720	CA	GLN C	54	26.265	56.691	29.378	1.00 50.29	6
	MOTA	3721	CB	GLM C	54	27.759	56.749	29.053	1.00 50.27	6
	MOTA	3722	CG	GLN C	54	28.231	58.111	28.587	1.00 54.00 1.00 55.07	6 6
	ATOM	3723	CD	GLN C	54	29.710 30.172	58.344 58.241	28.853 29.988	1.00 53.42	8
15	MOTA	3724	-	GLN C	54 54	30.172	58.667	27.805	1.00 57.05	7
15	ATOM	3725	NE2	GLN C	54	25.415	56.797	28.125	1.00 50.70	6
	ATOM	3726 3727	С О	GLN C	54	25.886	56.617	27.004	1.00 52.15	8
	ATOM ATOM	3728	N	GLN C	55	24.138	57.069	28.345	1.00 51.37	7
	MOTA	3729	CA	GLN C	55	23.169	57.205	27.272	1.00 54.41	6
20	ATOM	3730	CB	GLN C	55	21.786	57.326	27.897	1.00 57.18	6
	ATOM	3731	CG	GLN C	55	20.667	57.648	26.948	1.00 64.94	6
	ATOM	3732	CD	GLN C	55	19.313	57.472	27.617	1.00 70.65	6
	ATOM	3733		GLN C	55	19.154	57.760	28.817	1.00 73.87	8
	ATOM	3734		GLN C	55	18.325	56.997	26.849	1.00 72.08	7
25	ATOM	3735	C	GLN C	55	23.509	58.419	26.396	1.00 53.13	6
	MOTA	3736	0	GLN C	55	23.296	59.569	26.779	1.00 54.85	8
	ATOM	3737	N	THR C	56	24.044	58.148	25.211	1.00 50.27	7
	MOTA	3738	CA	THR C	56	24.455	59.193	24.290	1.00 48.20	6
	MOTA	3739	CB	THR C	56	25.916	59.019	23.905	1.00 47.97	6
30	MOTA	3740		THR C	56	26.693	58.795	25.085	1.00 51.04	8
	MOTA	3741	CG2		56	26.431	60.243	23.219	1.00 46.01	6 6
	MOTA	3742	C	THR C	56	23.633	59.162	23.023	1.00 49.71 1.00 49.78	8
	MOTA	3743	0	THR C	56	23.216	58.095 60.340	22.568 22.454	1.00 49.76	7
0.5	MOTA	3744	N	THR C	57 57	23.393 22.619	60.436	21.221	1.00 49.62	6
35	MOTA	3745	CA	THR C	57 57	21.122	60.592	21.501	1.00 49.45	6
	MOTA	3746 3747	CB OG1	THR C	57	20.640	59.440	22.206	1.00 49.55	8
	MOTA MOTA	3748	CG2		57	20.368	60.722	20.191	1.00 51.01	6
	ATOM	3749	C	THR C	57	23.057	61.608	20.368	1.00 48.68	6
40	ATOM	3750	Ö	THR C	57	23.423	62.649	20.888	1.00 51.05	8
	MOTA	3751	N	TRP C	58	23.033	61.428	19.056	1.00 45.80	7
	ATOM	3752	CA	TRP C	58	23.415	62.487	18.145	1.00 45.33	6
	MOTA	3753	СВ	TRP C	58	24.934	62.702	18.146	1.00 44.23	6
	MOTA	3754	CG	TRP C	58	25.733	61.584	17.556	1.00 45.68	6
45	MOTA	3755	CD2	TRP C	58	26.221	60.428	18.241	1.00 43.51	6
	ATOM	3756		TRP C	58	26.896	59.642	17.296	1.00 41.95	6
	MOTA	3757		TRP C	58	26.150	59.983	19.566	1.00 44.75	6
	MOTA	3758		TRP C	58	26.120	61.453	16.264	1.00 41.99	6
	MOTA	3759		TRP C	58	26.818	60.292	16.097	1.00 43.07 1.00 42.44	7 6
50	MOTA	3760		TRP C	58	27.498	58.436	17.625 19.894	1.00 45.66	6
	MOTA	3761		TRP C	58	26.748	58.778 58.020	18.926	1.00 44.08	6
	MOTA	3762		TRP C	58	27.414	62.107	16.772	1.00 46.80	6
	MOTA	3763		TRP C	58 58	22.915 22.315	61.054	16.603	1.00 45.26	8
55	MOTA	3764				23.157	62.959	15.788	1.00 50.21	7
55	MOTA	3765 3766		SER C		22.663	62.684	14.452	1.00 53.47	6
	MOTA MOTA	3765		SER C		21.536	63.657	14.128	1.00 54.42	6
	ATOM	3768		SER C		20.707	63.146	13.104	•	8
	ATOM	3769		SER C		23.733	62.752	13.376		6
60	MOTA	3770		SER C		24.541		13.343	1.00 54.12	8
	MOTA	3771		ASP C		23.727	61.745	12.503	1.00 57.21	7

							104				
							-134	C1 C4C	11 206	1.00 59.27	6
	MOTA	3772		ASP C	60		24.677	61.646	11.396	1.00 59.27	6
	ATOM	3773	CB	ASP C	60		25.680	60.517 60.472	11.650 10.615	1.00 53.02	6
	MOTA	3774	CG	ASP C	60		26.786 26.553	60.472	9.462	1.00 60.03	8
_	MOTA	3775		ASP C	60		26.333	59.996	10.957	1.00 62.69	8
5	MOTA	3776		ASP C	60		23.842	61.317	10.172	1.00 61.10	6
	ATOM	3777	C	ASP C	60 60		23.493	60.163	9.940	1.00 61.72	8
	ATOM	3778	0	ASP C	60 61		23.509	62.338	9.396	1.00 63.66	7
	MOTA	3779	N	ARG C	61		22.689	62.153	8.201	1.00 65.73	6
10	MOTA	3780	CA	ARG C	61		22.276	63.516	7.628	1.00 68.89	6
10	ATOM	3781	CB	ARG C	61		21.106	64.221	8.348	1.00 74.08	6
	MOTA	3782 3783	CG CD	ARG C	61		20.624	65.417	7.517	1.00 79.55	6
	MOTA	3784	NE	ARG C	61		19.438	66.085	8.059	1.00 84.63	7
	MOTA	3785	CZ	ARG C	61		18.810	67.101	7.457	1.00 87.07	6
15	MOTA MOTA	3786		ARG C	61		19.257	67.572	6.291	1.00 88.09	7
13	ATOM	3787		ARG C	61		17.721	67.636	8.005	1.00 87.40	7
	ATOM	3788	C	ARG C	61		23.322	61.310	7.083	1.00 64.92	6
	ATOM	3789	ō	ARG C	61		22.604	60.783	6.225	1.00 65.71	8
	ATOM	3790	N	THR C	62		24.648	61.176	7.078	1.00 62.18	7
20	MOTA	3791	CA	THR C	62		25.301	60.393	6.038	1.00 60.64	6
20	ATOM	3792	CB	THR C	62		26.840	60.568	6.056	1.00 61.65	6
	MOTA	3793		THR C	· 62		27.389	59.999	7.256	1.00 63.35	8
	MOTA	3794		THR C	62		27.207	62.045	5.983	1.00 61.52	6
	ATOM	3795	C	THR C	62		24.970	58.917	6.211	1.00 60.11	6
25	ATOM	3796	0	THR C	62		25.303	58.095	5.354	1.00 61.77	8
	ATOM	3797	N	LEU C	63		24.313	58.592	7.321	1.00 58.17	7
	ATOM	3798	CA	LEU C	63		23.919	57.219	7.621	1.00 57.53	6
	MOTA	3799	CB	LEU C			24.079	56.929	9.111	1.00 54.69	6 6
	MOTA	3800	CG	ren c			25.442	57.142	9.750	1.00 55.50 1.00 54.27	6
30	MOTA	3801		LEU C			25.327	56.938	11.263	1.00 54.27	6
	MOTA	3802	CD2	LEU C			26.449	56.178	9.139	1.00 58.42	6
	MOTA	3803	С	LEU C			22.455	56.977	7.242	1.00 58.94	8
	MOTA	3804	0	LEU C			22.010	55.830	7.147 7.037	1.00 58.80	7
	MOTA	3805	N	ALA C			21.707	58.055	6.703	1.00 50.00	6
35	MOTA	3806		ALA C			20.291	57.928 59.310	6.522	1.00 61.89	6
	MOTA	3807		ALA C			19.666 20.081	57.087	5.450	1.00 63.09	6
	MOTA	3808		ALA C			20.840	57.179	4.481	1.00 63.27	8
	MOTA	3809		ALA (19.055	56.249	5.485	1.00 65.02	7
40	MOTA	3810		TRP (18.749	55.381	4.355	1.00 66.31	6
40	MOTA	3811		TRP (19.329	53.989	4.600	1.00 64.14	6
	MOTA	3812		TRP			18.597	53.208	5.687	1.00 62.22	6
	MOTA	3813		2 TRP (18.962	53.110	7.074	1.00 57.97	6
	MOTA	3814 3815		2 TRP (18.025	52.247	7.694	1.00 56.42	6
45	MOTA MOTA	3816					19.985	53.666	7.848	1.00 55.52	6
40	MOTA	3817		1 TRP			17.475	52.430	5.533	1.00 60.23	6
	MOTA	3818		1 TRP		•	17.131	51.849	6.734	1.00 57.79	7
	MOTA	3819		2 TRP			18.088	51.926	9.049	1.00 55.30	6
	MOTA	3820	CZ	3 TRP	c 65		20.047	53.350	9.195	1.00 56.61	6
50	ATOM	382		2 TRP			19.102	52.484	9.784		6
	ATOM	3822		TRP			17.238		4.252		6
	ATOM	3823		TRP			16.540		5.268		8
	ATOM	3824		ASN	C 66		16.728		3.037	1.00 72.17	7
	ATOM	382		ASN	C 66		15.283		2.882		6
55	ATOM	382		ASN	C 66		14.863		1.408	1.00 77.34	6
	MOTA	382		ASN			13.355				6
	MOTA	382	8 OI	1 ASN			12.845				8 7
	MOTA	382	_	2 ASN			12.633				6
_	MOTA	383		ASN			14.802				8
60				ASN			15.431				7
	MOTA	383	2 N	SER	C 67		13.685	, ,,,,,,,,,	, 3,237		•

						-135				
	MOTA	3833	CA	SER C	67	13.166	52.647	4.920	1.00 73.52	6
	ATOM	3834	CB	SER C	67	13.451	52.759	6.411	1.00 72.63	6
	MOTA	3835	OG	SER C	67	12.985	53.994	6.914	1.00 70.04	8
	MOTA	3836	С	SER C	67	11.684	52.469	4.702	1.00 75.29	6
5	MOTA	3837	0	SER C	67	11.010	51.788	5.493	1.00 75.31	8
	MOTA	3838	N	SER C	68	11.165	53.077	3.639	1.00 77.57	7
	MOTA	3839	CA	SER C	68	9.739	52.957	3.356	1.00 78.39	6
	MOTA	3840	CB	SER C	68	9.327	53.874	2.187	1.00 77.79	6
40	ATOM	3841	OG	SER C	68	10.010	53.570	0.983	1.00 77.16	8 6
10	MOTA	3842	C	SER C	68	9.398	51.498	3.051	1.00 78.91 1.00 78.88	8
	MOTA	3843	0	SER C	68	8.242	51.165	2.802	1.00 78.88	7
	MOTA	3844	N	HIS C	69	10.415 10.252	50.634 49.197	3.090 2.824	1.00 81.55	6
	MOTA	3845	CA	HIS C	69 69	10.252	48.935	1.319	1.00 84.67	6
4 5	MOTA	3846	CB	HIS C	69	9.327	49.755	0.542	1.00 88.75	6
15	MOTA	3847	CG	HIS C	69	8.119	49.436	0.014	1.00 89.38	6
	MOTA	3848 3849		HIS C	69	9.479	51.115	0.359	1.00 89.98	7
	MOTA ATOM	3850		HIS C	69	8.405	51.600	-0.239	1.00 91.29	6
	ATOM ATOM	3851		HIS C	69	7.564	50.602	-0.458	1.00 91.72	7
20	ATOM	3852	C	HIS C	69	11.363	48,406	3.514	1.00 80.62	6
	ATOM	3853	ŏ	HIS C	69	11.740	47.318	3.072	1.00 79.15	8
	ATOM	3854	Ŋ	SER C	70	11.867	48.961	4.614	1.00 79.62	7
	ATOM	3855	CA	SER C	70	12.950	48.341	5.355	1.00 77.30	6
	ATOM	3856	СВ	SER C	70	14.262	48.818	4.739	1.00 77.47	6
25	ATOM	3857	OG	SER C	70	14.107	48.991	3.336	1.00 74.00	8
	MOTA	3858	С	SER C	70	12.880	48.746	6.836	1.00 76.56	6
	MOTA	3859	0	SER C	70	12.168	49.686	7.193	1.00 77.11	8
	MOTA	3860	N	PRO C	71	13.587	48.014	7.726	1.00 76.29	7
	MOTA	3861	CD	PRO C	71	14.305	46.733	7.544	1.00 75.52	6
30	MOTA	3862	CA	PRO C	71	13.538	48.401	9.143	1.00 74.74	6
	MOTA	3863	CB	PRO C	71	14.366	47.322	9.843	1.00 75.26 1.00 75.64	6 6
	MOTA	3864	CG	PRO C	71	14.241	46.124	8.936 9.235	1.00 73.64	6
	MOTA	3865	С	PRO C	71	14.202	49.771 50.125	8.401	1.00 73.01	8
0.5	MOTA	3866	0	PRO C	71	15.042	50.537	10.247	1.00 72.60	7
35	ATOM	3867	N	ASP C	72	13.828 14.377	51.869	10.414	1.00 70.96	6
	ATOM	3868	CA	ASP C	72 72	13.277	52.795	10.899	1.00 75.25	6
	MOTA	3869	CB	ASP C	72	11.919	52.353	10.415	1.00 78.33	6
	MOTA	3870	CG	ASP C	72	11.633	52.512	9.199	1.00 79.88	8
40	MOTA	3871 3872		ASP C	72	11.150	51.821	11.256	1.00 79.56	8
40	MOTA	3873	C C	ASP C	72	15.519	51.835	11.411	1.00 68.36	6
	MOTA MOTA	3874	Ö	ASP C		16.046	52.887	11.799	1.00 66.88	8
	ATOM	3875	N	GLN C	73	15.883	50.625	11.838	1.00 63.81	7
	MOTA	3876	CA	GLN C		17.001	50.485	12.756	1.00 61.20	6
45	ATOM	3877	СВ	GLN C		16.537	50.494	14.191	1.00 61.12	6
	ATOM	3878		GLN C		16.121		14.749	1.00 62.71	6
	MOTA	3879		GLN C		15.665	51.603	16.163	1.00 64.60	6
	ATOM	3880		L GLN C		14.784	50.779	16.421	1.00 67.49	8
	ATOM	3881	NE	GLN C	73	16.267		17.099	1.00 66.00	7
50	MOTA	3882	С	GLN C	73	17.842		12.583	1.00 59.70	6
	MOTA	3883	0	GLN C	73	17.350		12.213	1.00 61.26	8
	MOTA	3884	N	VAL C		19.122		12.893	1.00 56.05	7
	MOTA	3885	CA			20.050		12.825	1.00 52.11	6
	ATOM	3886		VAL C		20.736		11.454		6 6
55	MOTA	3887		1 VAL C		19.732		10.397 11.112		6
	MOTA	3888		2 VAL C		21.376		13.891		6
	ATOM	3889		VAL		21.095		14.332		8
	MOTA	3890		VAL C		21.277 21.754		14.323		7
60	ATOM	3891		SER C		22.809		15.318		6
60	MOTA	3892				22.784		16.257		6
	MOTA	3893	CB	DEK (. /3	22.104	40.557	,_,		

						-136				
	ATOM	3894	OG	SER C	75	21.818	46.521	17.269	1.00 43.99	8
	ATOM	3895	C	SER C	75	24.146	47.611	14.595	1.00 44.84	
	ATOM	3896	0	SER C	75	24.519	46.703	13.858	1.00 47.60	8
	MOTA	3897	N	VAL C	76	24.858	48.712	14.811	1.00 43.51	7
5	MOTA	3898	CA	VAL C	76	26.140	48.941	14.165	1.00 42.84	
	MOTA	3899	CB	VAL C	76	26.122	50.273	13.412	1.00 41.76	
	MOTA	3900	CG1	VAL C	76	27.441	50.504	12.741	1.00 42.71	
	MOTA	3901	CG2	VAL C	76	25.003	50.279	12.403	1.00 40.70	
	ATOM	3902	С	VAL C	76	27.294	48.961	15.153	1.00 42.64	
10	MOTA	3903	0	VAL C	76	27.194	49.542	16.227	1.00 45.77	
	ATOM	3904	N	PRO C	77	28.409	48.313	14.812	1.00 41.78	
	MOTA	3905	CD	PRO C	77	28.644	47.345	13.737	1.00 41.15 1.00 41.64	
	ATOM	3906	CA	PRO C	77 77	29.532 30.527	48.326 47.370	15.748 15.108	1.00 41.84	
15	MOTA	3907	CB	PRO C	77	29.654	47.370	14,379	1.00 40.47	
15	MOTA	3908	CG	PRO C PRO C	77	30.074	49.746	15.860	1.00 41.29	
	MOTA	3909 3910	С О	PRO C	77	30.123	50.489	14.881	1.00 38.61	
	MOTA MOTA	3911	И	ILE C	78	30.469	50.111	17.070	1.00 41.82	
	ATOM	3911	CA	ILE C	78	31.000	51.433	17.359	1.00 41.93	
20	ATOM	3912	CB	ILE C	78	31.439	51.489	18.837	1.00 42.16	
20	ATOM	3914	CG2	ILE C	78	32.370	52.634	19.107	1.00 42.14	
	ATOM	3915		ILE C	78	30.193	51.601	19.696	1.00 44.77	
	ATOM	3916		ILE C	78	29.251	52.676	19.216	1.00 44.16	6
	ATOM	3917	C	ILE C	78	32.149	51.813	16.450	1.00 42.57	7 6
25	ATOM	3918	ō	ILE C	78	32.287	52.963	16.063	1.00 45.18	
	ATOM	3919	N	SER C	79	32.963	50.829	16.100	1.00 43.18	
	MOTA	3920	CA	SER C	79	34.120	51.030	15.241	1.00 43.52	
	ATOM	3921	CB	SER C	79	34.969	49.768	15.242	1.00 43.74	
	ATOM	3922	OG	SER C	79	34.189	48.637	14.910	1.00 43.50	
30	MOTA	3923	С	SER C	79	33.810	51.415	13.804	1.00 43.43	
	MOTA	3924	0	SER C	79	34.698	51.838	13.082	1.00 44.10	
	MOTA	3925	N	SER C	80	32.562	51.264	13.380	1.00 43.63	
	MOTA	3926	CA	SER C	80	32.180	51.604	12.012	1.00 44.83	
	MOTA	3927	CB	SER C	80	31.260	50.534	11.441	1.00 44.2	
35	MOTA	3928	OG	SER C	80	31.915	49.284	11.380	1.00 52.55 1.00 46.5	
	MOTA	3929	C	SER C	80	31.482	52.956	11.908	1.00 46.1	
	ATOM	3930	0	SER C	80	31.050	53.355 53.649	10.829 13.035	1.00 46.4	
	MOTA	3931	N	LEU C	81	31.366 30.720	54.952	13.080	1.00 45.8	
40	MOTA	3932	CA	LEU C	81 81	29.467	54.891	13.935	1.00 45.0	
40	MOTA	3933	CB CG	LEU C	81	28.421	53.827	13.653	1.00 46.5	
	MOTA MOTA	3934 3935		LEU C	81	27.488	53.701	14.839	1.00 45.0	
	ATOM	3936		LEU C	81	27.667	54.198	12.405	1.00 47.6	9 6
	ATOM	3937	C	LEU C	81	31.645	55.973	13.718	1.00 46.1	
45	ATOM	3938	Õ			32.636	55.613	14.355	1.00 50.3	6 8
	ATOM	3939	N	TRP C	82	31.323	57.249	13.536	1.00 43.5	8 7
	MOTA	3940	CA	TRP C	82	32.086	58.303	14.161	1.00 39.7	
	MOTA	3941	СВ	TRP C	82	31.860	59.639	13.463	1.00 41.9	
	ATOM	3942	CG	TRP C	82	32.342	60.817	14.278	1.00 44.1	
50	MOTA	3943	CD2	TRP C	82	31.577	61.569	15.230	1.00 44.1	
	ATOM	3944	CE	TRP C	82	32.453	62.504	15.823	1.00 43.3	
	ATOM	3945	CE3		82	30.234	61.540	15.645	1.00 44.5	
	ATOM	3946		L TRP C	82	33.611	61.318	14.327	1.00 43.7	
	MOTA	3947	NE.		82	33.686	62.327	15.252	1.00 44.5	
55	MOTA	3948			82	32.033	63.405	16.809	1.00 42.6 1.00 43.2	
	MOTA	3949			82	29.818	62.430	16.623 17.195	1.00 43.2	
	MOTA	3950			82	30.717	63.352	17.195	1.00 43.7	
	MOTA	3951		TRP C	82	31.426	58.348 58.174	15.514	1.00 39.3	
60	MOTA	3952		TRP C VAL C	82 83	30.219 32.201	58.574	16.557	1.00 40.2	
90	MOTA	3953		VAL C	83	31.626	58.649	17.887	1.00 39.3	
	MOTA	3954	CA	ے بندہ	0.5	51.020	00.010			-

	W O 01/30	731								101,21	
						-137					
	MOTA	3955	СВ	VAL C	83	31.8	91 5	7.325	18.657	1.00 38.82	6
	MOTA	3956		VAL C	83	31.5	87 5	7.479	20.109	1.00 39.50	6
	MOTA	3957		VAL C	83	31.0		6.219		1.00 38.81	6
		3958	C	VAL C	83	32.2		9.860	18.624	1.00 40.30	6
5	ATOM		0	VAL C	83	33.3			18.428	1.00 41.45	8
5	MOTA	3959			84	31.3				1.00 38.82	7
	MOTA	3960	N	PRO C		29.9			19.644	1.00 40.83	6
	MOTA	3961	CD	PRO C	84				20.220	1.00 36.19	6
	MOTA	3962	CA	PRO C	84	31.8			21.058	1.00 37.66	6
	MOTA	3963	CB	PRO C	84	30.5			20.201	1.00 37.00	6
10	ATOM	3964	CG	PRO C	84	29.4		1.609		1.00 34.25	6
	MOTA	3965	С	PRO C	84	32.9	99 6	1.358	21.098	1.00 35.16	8
	MOTA	3966	0	PRO C	84	32.9		0.351	21.788	1.00 33.10	7
	MOTA	3967	N	ASP C	85	34.0	•	2.206	21.093		6
	MOTA	3968	CA	ASP C	85	35.1		51.949	21.909	1.00 34.67	6
15	ATOM	3969	CB	ASP C	85	36.4		52.588	21.270	1.00 35.95	
_	MOTA	3970	CG	ASP C	85	36.2		54.056	21.046	1.00 35.70	6
	MOTA	3971	OD1	ASP C	85	35.1	.59 6	54.468	20.662	1.00 34.85	8
	ATOM	3972		ASP C	85	37.2		64.798	21.238	1.00 38.52	8
	ATOM	3973	Č	ASP C	85	35.0	05 (62.452	23.326	1.00 36.34	6
20	ATOM	3974	Ö	ASP C	85	35.8	306	63.229	23.841	1.00 39.41	8
20	ATOM	3975	N	LEU C	86	33.9	941 (61.978	23.962	1.00 36.11	7
		3976	CA	LEU C	86	33.6		62.385	25.315	1.00 36.00	6
	MOTA	3977	CB	LEU C	86	32.2	208	61.904	25.678	1.00 35.07	6
	MOTA		CG	LEU C	86	31.0		62.464	24.806	1.00 36.71	6
0.5	MOTA	3978		LEU C	86	29.		61.912	25.240	1.00 31.87	6
25	MOTA	3979		LEU C	86	31.		63.974	24.910	1.00 35.41	6
	MOTA	3980			86	34.		61.870	26.337	1.00 36.89	6
	ATOM	3981	С	LEU C	86	35.		60.795	26.189	1.00 38.19	8
	MOTA	3982	0	LEU C		34.		62.648	27.391	1.00 38.71	7
	MOTA	3983	N	ALA C	87	35.		62.268	28.461	1.00 38.06	6
30	MOTA	3984	CA	ALA C	87			62.838	28.200	1.00 35.59	6
	MOTA	3985	CB	ALA C	87	37.		62.799	29.772	1.00 38.10	6
	MOTA	3986	С	ALA C	_	35.		63.891	29.815	1.00 37.91	8
	MOTA	3987	0	ALA C	_		586	62.013	30.833	1.00 39.52	7
	MOTA	3988	N	ALA C		35.			32.147	1.00 40.05	6
35	MOTA	3989	CA	ALA C	_		756	62.448	33.005	1.00 40.30	6
	MOTA	3990	CB	ALA C			356	61.250	32.771	1.00 41.63	6
	MOTA	3991	С	ALA C			939	63.169	33.195	1.00 41.71	8
	MOTA	3992	0	ALA C			912	62.545		1.00 42.71	7
	MOTA	3993	N	TYR C	89		852	64.492	32.799	1.00 41.60	6
40	MOTA	3994	CA	TYR C	89		904	65.350	33.330		6
	ATOM	3995		TYR C	89	36.	368	66.775	33.459	1.00 43.41	6
	MOTA	3996		TYR C	89	35.	976	67.422	32.149	1.00 48.68	6
	MOTA	3997		1 TYR C	89		.321	68.653	32.129	1.00 51.90	
	MOTA	3998		1 TYR C		34	.991	69.284	30.920	1.00 53.01	6
45	MOTA	3999		2 TYR C		36	.290	66.830	30.929	1.00 48.32	6
70	MOTA	4000) CE	2 TYR C	89	35	.966	67.449	29.726	1.00 52.45	6
	MOTA	4001				35	.318	68.678	29.730	1.00 53.45	6
		4002				35	.017	69.305	28.545	1.00 56.75	8
	MOTA	4002		TYR			. 527	64.914	34.657	1.00 40.68	6
5 0	MOTA	4004		TYR			.727	65.075	34.863	1.00 39.21	8
50		4009		ASN			.725	64.364	35.562	1.00 39.53	7
	MOTA						.265	63.952	36.848	1.00 39.15	6
	MOTA	4006					.476	64.603	37.989	1.00 38.99	6
	MOTA	400				_	.995	64.290	37.944		6
	MOTA						.355	64.378	36.902		8
55				O1 ASN			.443	63.939	39.090		
	MOTA			O2 ASN			.343	62.448	37.033		
	MOTA			ASN	_			61.946			
	MOTA				_		.354	61.733			
_	MOTA						.400	60.292			
60	MOTA (.528				
	ATOM	401	5 C	B ALA	C 91	37	.346	59.733	J-4.J2.		

	• • • • • • • • • • • • • • • • • •									
						-138				
	MOTA	4016	С	ALA C	91	38.939	60.033	36.435	1.00 39.96	6
	MOTA	4017	0	ALA C	91	39.898	60.664	36.007	1.00 35.60	8
		4018		ILE C	92	39.040	59.093	37.356	1.00 41.49	7
	MOTA		N		92	40.292	58.731	37.993	1.00 43.20	6
-	ATOM	4019	CA	ILE C		40.020	58.594	39.511	1.00 47.77	6
5	ATOM	4020	CB_	ILE C	92				1.00 47.77	6
	MOTA	4021		ILE C	92	39.923	57.130	39.921	1.00 50.98	6
	MOTA	4022		ILE C	92	41.093	59.293	40.316		
	MOTA	4023	CD1	ILE C	92	40.903	59.036	41.812	1.00 55.36	6
	MOTA	4024	С	ILE C	92	40.861	57.416	37.403	1.00 41.81	6
10	MOTA	4025	0	ILE C	92	41.973	56.992	37.720	1.00 40.19	8
	ATOM	4026	N	SER C	93	40.080	56.781	36.541	1.00 39.24	7
	ATOM	.4027	CA	SER C	93	40.470	55.534	35.913	1.00 39.09	6
	ATOM	4028	СВ	SER C	93	39.892	54.356	36.685	1.00 39.19	6
	ATOM	4029	OG	SER C	93	38.479	54.310	36.541	1.00 39.34	8
15		4030	C	SER C	93	39.839	55.579	34.546	1.00 37.69	6
15	ATOM				93	38.987	56.404	34.311	1.00 39.27	8
	MOTA	4031	0	SER C		40.251	54.717	33.632	1.00 37.58	7
	MOTA	4032	Ŋ	LYS C	94	39.612	54.737	32.330	1.00 40.65	6
	MOTA	4033	CA	LYS C	94		54.256	31.228	1.00 41.66	6
	ATOM	4034	CB	LYS C	94	40.560			1.00 46.32	6
20	ATOM	4035	CG	LYS C	94	41.383	53.024	31.520	1.00 48.62	6
	MOTA	4036	CD	LYS C	94	42.502	52.902	30.485		
	MOTA	4037	CE	LYS C	94	41.962	53.091	29.069	1.00 47.90	6
	ATOM	4038	NZ	LYS C	94	42.999	52.929	28.024	1.00 48.05	7
	ATOM	4039	С	LYS C	94	38.321	53.926	32.359	1.00 40.78	6
25	MOTA	4040	Ó	LYS C	94	38.102	53.094	33.234	1.00 42.52	8
	MOTA	4041	·N	PRO C	95	37.434	54.178	31.404	1.00 41.55	7
	ATOM	4042	CD	PRO C	95	37.555	55.150	30.312	1.00 42.12	6
		4043	CA	PRO C	95	36.153	53.479	31.335	1.00 41.34	6
	MOTA			PRO C	95	35.439	54.166	30.177	1.00 41.08	6
00	MOTA	4044	CB		95	36.125	55.476	30.058	1.00 42.87	6
30	ATOM	4045	CG	PRO C		36.256	52.000	31.102	1.00 40.86	6
	MOTA	4046	C	PRO C	95		51.563	30.189	1.00 41.65	8
	MOTA	4047	0	PRO C	95	36.941		31.940	1.00 40.55	7
	ATOM	4048	N	GLU C	96	35.581	51.228		1.00 41.10	6
	MOTA	4049	CA	GLU C	96	35.560	49.791	31.766	1.00 43.71	6
35	ATOM	4050	CB	GLU C	96	35.684	49.050	33.104	1.00 43.71	
	MOTA	4051	CG	GLU C	96	35.762	47.521	32.954	1.00 49.85	6
	ATOM	4052	CD	GLU C	96	35.912	46.768	34.286	1.00 54.35	6
	ATOM	4053	OE.	L GLU C	96	36.282	47.404	35.302	1.00 58.62	8
	ATOM	4054		2 GLU C		35.682	45.534	34.316	1.00 52.48	8
40	ATOM	4055		GLU C		34.190	49.553	31.168	1.00 39.91	6
40		4056		GLU C		33.200	49.478	31.894	1.00 40.62	8
	MOTA			VAL C		34.133	49.483	29.841	1.00 35.73	7
	ATOM	4057		VAL C		32.876	49.249	29.153	1.00 34.27	6
	MOTA	4058				33.006	49.541	27.660	1.00 31.66	6
	MOTA	4059		VAL C			49.333	26.968	1.00 34.09	6
45	MOTA	4060		1 VAL C		31.686		27.470	1.00 30.22	6
	MOTA	4061		2 VAL C		33.437	50.963		1.00 34.55	6
	MOTA	4062	C	VAL		32.481		29.382	1.00 34.33	
	MOTA	4063	0	VAL	97	33.167		28.949	1.00 35.63	8
	MOTA	4064	N	LEU C	98	31.362	47.607	30.072	1.00 35.35	7
50	MOTA	4065		LEU C	98	30.868		30.433	1.00 34.12	6
•	MOTA	4066		_		30.098	46.377	31.752	1.00 33.63	6
		4067		_		30.741		32.961	1.00 35.44	6
	MOTA			1 LEU (29.694		33.989	1.00 37.77	6
	MOTA	4068				31.806		33,538	1.00 34.23	6
	ATOM	4069		2 LEU (6
55	MOTA	4070		LEU (29.965				8
	MOTA	4073		LEU (29.640				7
	MOTA	4072	2 N	THR		29.567				6
	MOTA	407	3 CA	THR		28,642				
	MOTA	407	4 CE	THR	C . 99	27.317				6
60		407	5 00	1 THR	C · 99	27.574		_		8
	MOTA	407		2 THR		26.648	3 46.474	28.792	1.00 34.14	6

					-139				
	ATOM	4077	С	THR C 99	29.154	45.895	25.965	1.00 37.65	6
	ATOM	4078	ŏ	THR C 99	30.147	46.549	25.664	1.00 37.93	8
	MOTA	4079	N	PRO C 100	28.497	45.134	25.073	1.00 37.89	7
	ATOM	4080	CD	PRO C 100	27.443	44.145	25.364	1.00 40.71	6
5	ATOM	4081	CA	PRO C 100	28.874	45.065	23.667	1.00 37.03	6
	ATOM	4082	CB	PRO C 100	27.716	44.298	23.046	1.00 37.46	6
	MOTA	4083	CG	PRO C 100	27.402	43.316	24.094	1.00 38.27	6
	MOTA	4084	С	PRO C 100	28.963	46.476	23.139	1.00 38.41	6 8
4.0	MOTA	4085	0	PRO C 100	28.082	47.297	23.390	1.00 39.24 1.00 38.06	7
10	MOTA	4086	N	GLN C 101	30.026	46.772	22.412	1.00 38.06	6
	ATOM	4087	CA	GLN C 101	30.169 31.639	48.113 48.479	21.893 21.827	1.00 38.35	6
	ATOM	4088	CB	GLN C 101	32.140	48.846	23.195	1.00 43.58	6
	MOTA	4089	CG	GLN C 101 GLN C 101	33.633	48.822	23.291	1.00 47.06	6
15	ATOM ATOM	4090 4091	CD OF1	GLN C 101	34.315	49.497	22.533	1.00 51.61	8
13	ATOM	4091	NE2		34.160	48.041	24.227	1.00 48.13	7
	MOTA	4093	C	GLN C 101	29.471	48.333	20.571	1.00 38.37	6
	ATOM	4094	Ö	GLN C 101	30.095	48.620	19.554	1.00 36.55	8
	ATOM	4095	N	LEU C 102	28.148	48.198	20.627	1.00 40.04	7
20	ATOM	4096	CA	LEU C 102	27.263	48.373	19.478	1.00 40.82	6
_	ATOM	4097	CB.	LEU C 102	26.376	47.143	19.289	1.00 38.65	6
	MOTA	4098	CG	LEU C 102	27.061	45.791	19.163	1.00 40.16	6
	MOTA	4099		LEU C 102	26.015	44.708	18.994	1.00 37.69	6
	ATOM	4100	CD2	LEU C 102	27.991	45.815	17.981	1.00 39.89	6 6
25	MOTA	4101	C	LEU C 102	26.362	49.583	19.685	1.00 40.48 1.00 39.50	8
	MOTA	4102	0	LEU C 102	25.940	49.880	20.800 18.603	1.00 39.50	7
	MOTA	4103	N	ALA C 103	26.072 25.203	50.280 51.434	18.674	1.00 42.17	6
	ATOM	4104	CA	ALA C 103	25.879	52.646	18.054	1.00 43.90	6
30	ATOM	4105 4106	CB C	ALA C 103 ALA C 103	23.950	51.087	17.904	1.00 43.55	6
30	ATOM ATOM	4107	o	ALA C 103	23.905	50.092	17.189	1.00 44.89	8
	MOTA	4108	N	ARG C 104	22.930	51.916	18.048	1.00 45.38	7
	MOTA	4109	CA	ARG C 104	21.674	51.689	17.359	1.00 46.54	6
	ATOM	4110	CB	ARG C 104	20.549	51.665	18.381	1.00 46.10	6
35	ATOM	4111	CG	ARG C 104	19.292	51.040	17.879	1.00 47.91	6
- •	ATOM	4112	CD	ARG C 104	19.457	49.560	17.559	1.00 45.29	6
	MOTA	4113	NE	ARG C 104	18.188	49.059	17.035	1.00 46.68	7 6
	MOTA	4114	CZ	ARG C 104	17.927	47.792	16.761	1.00 46.66	7
	MOTA	4115		ARG C 104	18.850	46.866	16.954	1.00 47.05 1.00 48.97	7
40	MOTA	4116		ARG C 104	16.733	47.452	16.308 16.367	1.00 46.82	6
	MOTA	4117	C	ARG C 104	21.491 21.550	52.830 53.999	16.738	1.00 49.29	8
	ATOM	4118	0	ARG C 104	21.296	52.501	15.098	1.00 47.65	7
	MOTA	4119	N	VAL C 105 VAL C 105	21.138	53.543	14.092	1.00 47.99	6
45	MOTA MOTA	4120 4121	CA CB	VAL C 105	22.200	53.426	12.980	1.00 46.29	6
45	ATOM	4122		VAL C 105	22.080	54.588	12.021	1.00 44.96	6
	ATOM	4123		2 VAL C 105	23.583	53.386	13.580	1.00 42.95	6
	ATOM	4124		VAL C 105	19.769	53.519	13.444	1.00 50.20	6
	ATOM	4125		VAL C 105	19.340	52.497	12.904	1.00 50.01	8
50	ATOM	4126		VAL C 106	19.097	54.666	13.506	1.00 51.90	7
	ATOM	4127		VAL C 106	17.767	54.836	12.933	1.00 53.33	6
	MOTA	4128	CB	VAL C 106	16.947	55.840	13.758	1.00 51.93	6
	MOTA	4129		1 VAL C 106	15.503	55.825	13.306 15.222	1.00 49.94 1.00 50.56	6 6
	MOTA	4130		2 VAL C 106	17.060	55.504	15.222	1.00 50.56	6
55	MOTA	4131		VAL C 106	17.899	55.347 56.151	11.497	1.00 52.33	8
	MOTA	4132		VAL C 106	18.782 17.016	54.889	10.615		7
	MOTA	4133		SER C 107	17.016	55.275	9.208		6
	MOTA	4134 4135			15.835	54.734			6
60	ATOM ATOM	4136			14.672	54.943		1.00 59.41	8
00	MOTA	4137		SER C 107	17.228	56.762	_	1.00 56.30	6
			_						

ATOM 4138 O SER C 107 ATOM 4139 N ASP C 108 ATOM 4140 CA ASP C 108 ATOM 4141 CB ASP C 108 ATOM 4141 CB ASP C 108 ATOM 4142 CG ASP C 108 ATOM 4143 ODI ASP C 108 ATOM 4143 ODI ASP C 108 ATOM 4143 ODI ASP C 108 ATOM 4144 CB ASP C 108 ATOM 4143 ODI ASP C 108 ATOM 4145 CA ASP C 108 ATOM 4145 CC ASP C 108 ATOM 4146 CB ASP C 108 ATOM 4147 N GLY C 109 ATOM 4146 CB ASP C 108 ATOM 4149 C GLY C 109 ATOM 4149 C GLY C 109 ATOM 4149 C GLY C 109 ATOM 4151 N GLU C 110 ATOM 4151 N GLU C 110 ATOM 4152 CB GLU C 110 ATOM 4155 CB GLU C 110 ATOM 4157 CB GLU C 110 ATOM 4157 CB GLU C 110 ATOM 4158 CB GLU C 110 ATOM 4157 CB GLU C 110 ATOM 4157 CB GLU C 110 ATOM 4158 CB GLU C 110 ATOM 4157 CB GLU C 110 ATOM 4158 CB GLU C 110 ATOM 4157 CB GLU C 110 ATOM 4158 CB GLU C 110 ATOM 4157 CB GLU C 110 ATOM 4158 CB GLU C 110 ATOM 4168 CB							-140				
ATOM 4139 N ASP C 108 ATOM 4140 CA ASP C 108 ATOM 4141 CS ASP C 108 ATOM 4141 CS ASP C 108 ATOM 4142 CG ASP C 108 ATOM 4142 CG ASP C 108 ATOM 4143 ODI ASP C 108 ATOM 4143 ODI ASP C 108 ATOM 4144 ODI ASP C 108 ATOM 4144 ODI ASP C 108 ATOM 4145 ODI ASP C 108 ATOM 4145 ODI ASP C 108 ATOM 4146 O ASP C 108 ATOM 4147 ODI ASP C 108 ATOM 4146 O ASP C 108 ATOM 4148 ODI ASP C 108 ATOM 4149 CA ASP C 108 ATOM 4149 CA ASP C 108 ATOM 4149 CA GLIY C 109 ATOM 4150 O GLIY C 109 ATOM 4151 ODI ASP C 108 ATOM 4150 O GLIY C 109 ATOM 4151 ODI ASP C 108 ATOM 4152 CA GLIY C 109 ATOM 4154 CG GLIY C 109 ATOM 4155 ODI GLIY C 109 ATOM 4155 ODI GLIY C 109 ATOM 4156 ODI GLIY C 109 ATOM 4156 ODI GLIY C 109 ATOM 4157 ODI ASP C 108 ATOM 4158 C GLIY C 109 ATOM 4156 ODI GLIY C 109 ATOM 4156 ODI GLIY C 110 ATOM 4157 ODI ASP C 108 ATOM 4158 C GLIY C 110 ATOM 4159 ODI GLIY C 110 ATOM 4159 ODI GLIY C 110 ATOM 4159 ODI GLIY C 110 ATOM 4158 C GLIY C 110 ATOM 4159 C GLIY C 110 ATOM 4159 C GLIY C 110 ATOM 4159 C GLIY C 111 ATOM 4158 C GLIY C 110 ATOM 4159 C GLIY			4120		C 107			57.129	7.797	1.00 55.13	8
ATOM 4140 CA ASP C 108				0 5	SER C 107				9.849	1.00 56.72	
ATOM									9.632		
5 ATOM 4142 CG ASP C 108								59.807	10.353	1.00 59.64	
ATOM 4143 OD1 ASP C 108 16.432 58.693 12.378 10.0 51.30 5 8 ATOM 4145 C ASP C 108 18.345 59.648 10.054 1.00 58.33 6 6 ATOM 4147 N GLY C 109 19.299 58.785 10.396 1.00 59.41 7 ATOM 4147 N GLY C 109 20.802 59.467 12.271 1.00 59.58 6 ATOM 4145 C GLY C 109 20.802 59.467 12.271 1.00 59.58 6 ATOM 4145 N GLY C 109 20.802 59.467 12.271 1.00 59.58 6 ATOM 4150 O GLY C 109 20.802 59.467 12.271 1.00 59.58 6 ATOM 4150 O GLY C 109 20.802 59.467 12.271 1.00 59.58 6 ATOM 4150 O GLY C 109 20.802 59.467 12.271 1.00 59.58 6 ATOM 4150 O GLY C 110 19.775 59.165 13.064 1.00 59.04 7 ATOM 4151 N GLU C 110 19.775 59.165 13.064 1.00 59.04 7 ATOM 4151 N GLU C 110 19.775 59.165 13.064 1.00 59.04 7 ATOM 4154 CG GLU C 110 18.481 59.327 15.141 1.00 62.39 6 ATOM 4155 CO GLU C 110 18.640 62.107 15.33 1.00 66.23 6 ATOM 4155 CO GLU C 110 18.640 62.107 15.33 1.00 66.23 6 ATOM 4156 OE1 GLU C 110 18.640 62.107 15.33 1.00 66.23 6 ATOM 4158 C GLU C 110 20.677 58.141 15.038 1.00 59.61 6 ATOM 4158 C GLU C 110 20.677 58.141 15.038 1.00 59.61 6 ATOM 4160 N VAL C 111 21.600 58.49 15.593 1.00 59.61 6 ATOM 4161 CA VAL C 111 21.600 58.49 15.593 1.00 59.61 6 ATOM 4163 CG VAL C 111 23.926 57.620 16.200 1.00 55.43 6 ATOM 4163 CG VAL C 111 24.105 57.706 14.686 1.00 55.43 6 ATOM 4163 CG VAL C 111 24.105 57.706 14.686 1.00 55.43 6 ATOM 4163 CG VAL C 111 22.328 58.373 18.706 1.00 55.43 6 ATOM 4163 CG VAL C 111 22.328 58.373 18.706 1.00 53.62 6 ATOM 4167 CG LEU C 112 2.308 57.337 18.048 1.00 54.63 6 ATOM 4167 CG LEU C 112 2.308 57.337 18.048 1.00 53.62 6 ATOM 4177 CB LEU C 112 2.308 57.337 18.706 1.00 53.62 6 ATOM 4177 CB LEU C 112 2.308 57.337 18.706 1.00 53.62 6 ATOM 4179 CD LEU C 112 2.308 57.337 18.706 1.00 53.62 6 ATOM 4179 CD LEU C 112 2.308 57.337 18.706 1.00 53.62 6 ATOM 4179 CD LEU C 112 2.308 57.337 18.706 1.00 53.62 6 ATOM 4179 CD LEU C 112 2.308 57.337 18.706 1.00 53.62 6 ATOM 4179 CD LEU C 112 2.308 57.337 18.706 1.00 53.62 6 ATOM 4179 CD LEU C 112 2.308 57.337 18.706 1.00 53.62 6 ATOM 4189 C BLU C 112 2.308 57.337 18.706 1.00 53.62 6 ATOM 4189 C BLU C 1	5									1.00 60.59	
ATOM 4144 ODZ ASP C 108	•			OD1 A	ASP C 108						
ATOM 4146 C ASP C 108			4144							1.00 63.04	
ATOM 4148 O GLY C 109		MOTA	4145								
ATOM ATOM ATOM ATOM ATOM ATOM ATOM ATOM	4.0									1.00 59.41	7
ATOM 4169 C GLY C 109 20.802 59.467 12.271 1.00 59.58 6 ATOM 4150 O GLY C 109 21.868 59.926 12.695 1.00 59.07 8 ATOM 4151 N GLU C 110 19.775 59.165 13.064 1.00 59.04 7 ATOM 4152 CA GLU C 110 19.871 59.325 14.508 1.00 59.38 6 ATOM 4152 CB GLU C 110 19.871 59.325 14.508 1.00 59.38 6 ATOM 4154 CG GLU C 110 18.481 59.327 15.141 1.00 62.39 6 ATOM 4155 CD GLU C 110 18.386 60.020 16.513 1.00 66.23 6 ATOM 4155 CD GLU C 110 18.717 61.520 16.441 1.00 70.42 6 ATOM 4156 OEI GLU C 110 18.640 62.107 15.333 1.00 69.27 8 ATOM 4158 C GLU C 110 20.677 58.141 15.038 1.00 77.225 8 ATOM 4159 O GLU C 110 20.677 58.141 15.038 1.00 59.61 6 ATOM 4150 CB VAL C 111 22.444 57.379 16.535 1.00 55.43 6 ATOM 4161 CA VAL C 111 22.444 57.379 16.535 1.00 55.43 6 ATOM 4163 CGI VAL C 111 23.926 57.620 16.200 1.00 55.47 6 ATOM 4166 C VAL C 111 22.328 58.373 18.706 1.00 53.14 6 ATOM 4166 C VAL C 111 22.328 57.337 18.048 1.00 54.63 6 ATOM 4166 C VAL C 111 22.328 58.373 18.706 1.00 53.67 8 ATOM 4166 C VAL C 111 22.328 55.599 20.034 1.00 54.63 6 ATOM 4170 CG LEU C 112 22.505 55.992 20.034 1.00 53.67 8 ATOM 4170 CG LEU C 112 22.350 55.992 20.034 1.00 54.63 6 ATOM 4171 CDI LEU C 112 23.926 57.620 16.200 1.00 53.62 6 ATOM 4170 CG LEU C 112 23.926 57.620 10.00 53.62 6 ATOM 4171 CDI LEU C 112 23.926 57.620 10.00 53.62 6 ATOM 4170 CG LEU C 112 23.926 57.620 10.00 53.62 6 ATOM 4171 CDI LEU C 112 23.926 57.620 10.00 53.62 6 ATOM 4171 CDI LEU C 112 23.926 57.620 10.00 53.62 6 ATOM 4174 CDI LEU C 112 23.926 57.620 10.00 53.62 6 ATOM 4176 CA TYR C 113 24.947 54.909 22.134 1.00 64.84 6 ATOM 4176 CA TYR C 113 24.947 54.909 22.134 1.00 64.85 6 ATOM 4180 CE TYR C 113 24.947 54.909 22.134 1.00 64.85 6 ATOM 4181 CD TYR C 113 24.937 53.509 27.700 1.00 47.87 6 ATOM 4181 CD TYR C 113 30.666 57.99 1.00 47.87 6 ATOM 4181 CD TYR C 113 30.666 57.99 1.00 47.40 7 ATOM 4188 CA HEU C 112 23.926 57.320 22.3310 1.00 40.85 6 ATOM 4189 CB MET C 114 22.497 54.909 22.134 1.00 40.85 6 ATOM 4189 CB MET C 114 22.498 53.559 27.700 1.00 48.89 6 ATOM 4189	10							-		1.00 58.66	6
ATOM 4151 N GLU C 110 19.775 59.165 13.064 1.00 59.04 7 ATOM 4152 CA GLU C 110 19.871 59.325 14.508 1.00 59.04 7 ATOM 4153 CB GLU C 110 18.864 0.020 16.513 1.00 62.39 6 ATOM 4155 CD GLU C 110 18.775 59.165 13.064 1.00 59.08 62.39 6 ATOM 4155 CD GLU C 110 18.776 61.520 16.441 1.00 70.42 6 ATOM 4156 CB LGU C 110 18.717 61.520 16.441 1.00 70.42 6 ATOM 4157 OB2 GLU C 110 20.677 78.141 15.038 1.00 69.27 8 ATOM 4158 C GLU C 110 20.677 78.141 15.038 1.00 69.27 8 ATOM 4159 O GLU C 110 20.677 78.141 15.038 1.00 59.61 6 ATOM 4159 O GLU C 110 20.677 78.141 15.038 1.00 59.61 6 ATOM 4160 N VAL C 111 22.044 57.379 16.555 1.00 55.71 6 ATOM 4161 CA VAL C 111 22.444 57.379 16.555 1.00 55.71 6 ATOM 4164 CG2 VAL C 111 24.783 56.511 16.788 1.00 59.61 6 ATOM 4165 C VAL C 111 24.783 56.511 16.788 1.00 55.71 6 ATOM 4166 C VAL C 111 22.308 57.337 18.006 1.00 55.71 6 ATOM 4166 C VAL C 111 22.308 57.337 18.006 1.00 55.07 6 ATOM 4167 N LEU C 112 22.328 58.373 18.706 1.00 55.04 6 ATOM 4167 N LEU C 112 22.050 55.992 20.034 1.00 53.09 7 ATOM 4167 N LEU C 112 22.050 55.992 20.034 1.00 53.09 7 ATOM 4167 N LEU C 112 22.050 55.992 20.034 1.00 50.60 4 6 ATOM 4175 C B LEU C 112 23.085 55.588 20.420 1.00 56.64 6 ATOM 4176 C B LEU C 112 23.085 55.588 20.420 1.00 56.64 6 ATOM 4176 C B LEU C 112 23.085 55.588 20.420 1.00 56.64 6 ATOM 4176 C B LEU C 112 23.053 54.963 20.452 1.00 53.28 6 ATOM 4176 C B LEU C 112 23.053 54.963 20.452 1.00 53.28 6 ATOM 4176 C B LEU C 112 23.053 54.963 20.424 1.00 54.81 8 ATOM 4176 C B LEU C 112 23.053 54.963 20.452 1.00 53.28 6 ATOM 4177 C B TYR C 113 24.945 55.207 18.374 1.00 62.31 6 ATOM 4180 C B TYR C 113 24.945 55.207 18.374 1.00 62.31 6 ATOM 4180 C B TYR C 113 24.945 55.207 18.374 1.00 62.31 6 ATOM 4180 C B TYR C 113 24.945 55.207 18.374 1.00 63.32 6 ATOM 4180 C B TYR C 113 24.945 55.207 18.374 1.00 64.83 6 ATOM 4180 C B TYR C 113 24.945 55.207 18.374 1.00 64.83 6 ATOM 4180 C B TYR C 113 24.945 55.207 18.374 1.00 64.83 6 ATOM 4180 C B TYR C 113 24.945 55.207 18.374 1.00 64.83 6 ATOM 4180 C B TYR C 113 24.945 55.207 1				CA	GIN C 109				12.271	1.00 59.58	
ATOM 4151 N GLU C 110 19.775 59.165 13.064 1.00 59.38 6								59.926			
15							19.775				
ATOM 4153 CB GLU C 110 ATOM 4154 CG GLU C 110 ATOM 4155 CD GLU C 110 ATOM 4155 CD GLU C 110 ATOM 4155 CD GLU C 110 ATOM 4156 OPE GLU C 110 ATOM 4157 OPE GLU C 110 ATOM 4158 C GLU C 110 ATOM 4159 OPE GLU C 110 ATOM 4159 OPE GLU C 110 ATOM 4159 OPE GLU C 110 ATOM 4160 N VAL C 111 ATOM 4161 CA VAL C 111 ATOM 4161 CA VAL C 111 ATOM 4166 CA VAL C 111 ATOM 4166 CB VAL C 111 ATOM 4167 OPE VAL C 111 ATOM 4168 CB VAL C 111 ATOM 4168 CB VAL C 111 ATOM 4169 CB LEU C 112 ATOM 4171 CD LEU C 112 ATOM 4171 CD LEU C 112 ATOM 4176 CA TYR C 113 ATOM 4176 CA TYR C 113 ATOM 4176 CA TYR C 113 ATOM 4177 CB TYR C 113 ATOM 4178 CG TYR C 113 ATOM 4179 CD TYR C 113 ATOM 4188 CA MET C 114 ATOM 4197 CB PRO C 115 ATOM 4199 CB PRO C 115 ATOM 4191 CB PRO C 115 ATOM 4199 CB PRO C	15			CA	GLU C 110						
ATOM 4155 CD GUU C 110 ATOM 4155 OD GUU C 110 ATOM 4155 OD GUU C 110 ATOM 4156 OEI GUU C 110 ATOM 4157 O2E GLU C 110 ATOM 4157 O2E GLU C 110 ATOM 4157 O2E GLU C 110 ATOM 4159 OEI GUU C 110 ATOM 4150 N VAL C 111 ATOM 4160 N VAL C 111 ATOM 4161 CA VAL C 111 ATOM 4161 CA VAL C 111 ATOM 4163 CGI VAL C 111 ATOM 4164 CE WAL C 111 ATOM 4165 C VAL C 111 ATOM 4166 O VAL C 111 ATOM 4167 N LEU C 112 ATOM 4168 CA LEU C 112 ATOM 4169 CB LEU C 112 ATOM 4169 CB LEU C 112 ATOM 4170 CG LEU C 112 ATOM 4170 CG LEU C 112 ATOM 4171 CD LEU C 112 ATOM 4171 CD LEU C 112 ATOM 4172 CD LEU C 112 ATOM 4175 N TYR C 113 ATOM 4176 CA TYR C 113 ATOM 4177 CB TYR C 113 ATOM 4177 CB TYR C 113 ATOM 4177 CB TYR C 113 ATOM 4180 CEI TYR C 113 ATOM 4180 CEI TYR C 113 ATOM 4181 CC TYR C 113 ATOM 4182 CC TYR C 113 ATOM 4184 CO TYR C 113 ATOM 4185 C TYR C 113 ATOM 4186 CA TYR C 113 ATOM 4187 CA TYR C 113 ATOM 4188 CA TYR C 113 ATOM 4189 CB TYR C 113 ATOM 4180 CC TYR				CB	GLU C 110						
ATOM 4156 OEI GUU C 110 ATOM 4157 OE2 GLU C 110 ATOM 4157 OE2 GLU C 110 ATOM 4157 OE2 GLU C 110 ATOM 4158 C GLU C 110 ATOM 4159 O GLU C 110 ATOM 4159 O GLU C 110 ATOM 4159 O GLU C 110 ATOM 4150 N VAL C 111 20.467 56.995 14.623 1.00 69.95 8 ATOM 4161 CA VAL C 111 22.444 57.379 16.535 1.00 57.63 7 ATOM 4163 CGI VAL C 111 24.783 56.511 16.788 1.00 55.43 6 ATOM 4166 CQ VAL C 111 24.105 57.706 14.686 1.00 55.43 6 ATOM 4166 C VAL C 111 22.328 57.337 18.048 1.00 53.64 6 ATOM 4166 C VAL C 111 22.328 57.337 18.048 1.00 53.67 8 ATOM 4166 C VAL C 111 22.328 57.337 18.048 1.00 53.67 8 ATOM 4168 CA LEU C 112 22.050 55.992 20.034 1.00 53.66 6 ATOM 4170 C GLEU C 112 19.380 56.011 19.557 1.00 60.85 6 ATOM 4171 CDI LEU C 112 19.439 57.490 19.341 1.00 52.22 6 ATOM 4173 C LEU C 112 23.053 55.548 20.420 1.00 53.28 6 ATOM 4176 CA TYR C 113 22.304 55.309 22.134 1.00 62.31 6 ATOM 4178 CG TYR C 113 22.304 55.309 22.134 1.00 62.41 6 ATOM 4171 CDI LEU C 112 23.053 55.4963 20.542 1.00 53.28 6 ATOM 4178 CG TYR C 113 22.304 55.309 22.134 1.00 62.41 6 ATOM 4178 CG TYR C 113 22.304 55.508 22.003 1.00 50.87 7 ATOM 4178 CG TYR C 113 22.024 55.207 18.374 1.00 62.41 6 ATOM 4178 CG TYR C 113 22.024 55.207 22.030 1.00 40.84 6 ATOM 4178 CG TYR C 113 22.024 55.609 22.134 1.00 50.87 7 ATOM 4178 CG TYR C 113 22.024 55.609 22.134 1.00 50.87 7 ATOM 4178 CG TYR C 113 22.024 55.609 22.134 1.00 40.84 6 ATOM 4180 CEI TYR C 113 22.024 55.609 22.134 1.00 40.84 6 ATOM 4181 CD2 TYR C 113 29.720 53.562 23.100 1.00 40.86 6 ATOM 4188 CA MET C 114 24.485 51.360 26.579 1.00 48.88 6 ATOM 4189 CB MET C 114 22.899 53.556 23.300 26.040 1.00 47.94 6 ATOM 4190 CG MET C 114 22.899 53.556 27.706 1.00 47.94 6 ATOM 4191 C MET C 114 22.895 55.399 26.440 1.00 47.94 6 ATOM 4191 C MET C 114 24.885 51.360 26.579 1.00 48.95 6 ATOM 4197 CA PROC 115 27.188 55.51 56.270 66 1.00 47.94 6 ATOM 4198 C MET C 114 24.885 51.360 26.579 1.00 48.95 6 ATOM 4197 CA PROC 115 27.188 53.771 1.500 48.99 6		MOTA	4154							1.00 70.42	
ATOM 4157 OB2 GLU C 110 ATOM 4158 C GLU C 110 ATOM 4159 O GLU C 110 ATOM 4159 O GLU C 110 ATOM 4159 O GLU C 110 ATOM 4160 N VAL C 111 21.600 58.419 15.953 1.00 55.43 6 ATOM 4161 CA VAL C 111 22.444 57.797 16.535 1.00 55.43 6 ATOM 4162 CB VAL C 111 23.926 57.620 16.200 1.00 55.71 6 ATOM 4163 CG1 VAL C 111 ATOM 4164 CG2 VAL C 111 ATOM 4165 C VAL C 111 ATOM 4166 O VAL C 111 22.308 57.307 18.048 1.00 53.14 6 ATOM 4167 N LEU C 112 22.308 57.337 18.048 1.00 53.67 8 ATOM 4168 CA LEU C 112 22.308 57.337 18.048 1.00 53.67 8 ATOM 4169 CB LEU C 112 22.050 55.992 20.034 1.00 53.62 6 ATOM 4169 CB LEU C 112 ATOM 4169 CB LEU C 112 ATOM 4170 CG LEU C 112 ATOM 4171 CD LEU C 112 ATOM 4172 CD LEU C 112 ATOM 4173 CD LEU C 112 ATOM 4174 CD LEU C 112 ATOM 4175 N TYR C 113 ATOM 4176 CB TYR C 113 ATOM 4177 CB TYR C 113 ATOM 4178 CC TYR C 113 ATOM 4179 CD TYR C 113 ATOM 4180 CEL TYR C 113 ATOM 4180 CEL TYR C 113 ATOM 4181 CD TYR C 113 ATOM 4181 CD TYR C 113 ATOM 4180 CEL TYR C 113 ATOM 4181 CD TYR C 113 ATOM 4180 CEL TYR C 113 ATOM 4181 CD TYR C 113 ATOM 4180 CEL TYR C 113 ATOM 4181 CD TYR C 113 ATOM 4180 CEL TYR C 113 ATOM 4180 CE		MOTA									8
ATOM 4158 C GLU C 110 20.677 58.141 15.038 1.00 59.61 6 ATOM 4159 O GLU C 110 20.467 56.995 14.623 1.00 60.95 8 ATOM 4160 N VAL C 111 21.600 58.419 15.953 1.00 57.63 7 ATOM 4161 CA VAL C 111 22.444 57.379 16.535 1.00 55.71 6 ATOM 4163 CGI VAL C 111 24.783 56.511 16.788 1.00 55.71 6 ATOM 4163 CGI VAL C 111 24.783 56.511 16.788 1.00 55.71 6 ATOM 4165 C VAL C 111 24.105 57.706 14.686 1.00 56.04 6 ATOM 4166 O VAL C 111 22.308 57.337 18.048 1.00 53.67 8 ATOM 4166 CO VAL C 111 22.308 57.337 18.048 1.00 54.63 6 ATOM 4166 CO VAL C 111 22.308 57.337 18.048 1.00 54.63 6 ATOM 4168 CA LEU C 112 22.050 55.992 20.034 1.00 53.62 6 ATOM 4169 CB LEU C 112 22.050 55.992 20.034 1.00 53.62 6 ATOM 4170 CG LEU C 112 19.380 56.011 19.657 1.00 60.85 6 ATOM 4171 CD1 LEU C 112 19.380 56.011 19.657 1.00 60.85 6 ATOM 4171 CD1 LEU C 112 19.439 57.490 19.341 1.00 62.41 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 50.87 7 ATOM 4175 CB TYR C 113 24.947 54.502 22.003 1.00 40.84 6 ATOM 4176 CA TYR C 113 24.947 54.502 22.003 1.00 40.84 6 ATOM 4177 CB TYR C 113 24.947 54.502 22.003 1.00 40.84 6 ATOM 4180 CE1 TYR C 113 27.428 52.716 22.181 1.00 39.26 6 ATOM 4180 CE1 TYR C 113 27.428 52.716 22.181 1.00 39.26 6 ATOM 4180 CE1 TYR C 113 28.663 54.710 22.602 1.00 41.46 6 ATOM 4187 N MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4189 CB MET C 114 22.809 53.375 25.910 1.00 40.68 6 ATOM 4187 N MET C 114 22.809 53.375 25.910 1.00 40.70 8 ATOM 4189 CB MET C 114 22.809 53.375 25.910 1.00 47.83 8 ATOM 4180 CA MET C 114 22.809 53.375 25.910 1.00 47.83 8 ATOM 4180 CA MET C 114 22.809 53.375 25.910 1.00 47.83 8 ATOM 4189 CB MET C 114 22.809 53.375 25.910 1.00 47.83 8 ATOM 4189 CB MET C 114 22.809 53.375 25.910 1.00 40.68 6 ATOM 4191 SD MET C 114 22.809 53.375 25.910 1.00 49.35 6 ATOM 4194 O MET C 114 22.809 53.375 25.910 1.00 47.83 6				OEL	GLU C 110					1.00 72.25	8
ATOM 4159 O GIJU C 110 20.467 56.995 14.623 1.00 60.95 8 ATOM 4161 N VAL C 111 21.600 58.419 15.953 1.00 57.63 7 ATOM 4161 CA VAL C 111 22.444 57.379 16.535 1.00 57.63 7 ATOM 4161 CA VAL C 111 22.444 57.379 16.535 1.00 55.43 6 ATOM 4162 CB VAL C 111 24.783 56.511 16.788 1.00 55.43 6 ATOM 4164 CG2 VAL C 111 24.783 56.511 16.788 1.00 53.14 6 ATOM 4164 CG2 VAL C 111 24.783 56.511 16.788 1.00 53.14 6 ATOM 4165 C VAL C 111 22.308 57.307 18.048 1.00 53.67 8 ATOM 4166 C VAL C 111 22.308 57.337 18.048 1.00 53.67 8 ATOM 4167 N LEU C 112 22.328 58.373 18.046 1.00 53.67 8 ATOM 4168 CA LEU C 112 22.050 55.992 20.034 1.00 53.62 6 ATOM 4170 CG LEU C 112 20.638 55.548 20.420 1.00 56.64 6 ATOM 4170 CG LEU C 112 19.380 56.011 19.657 1.00 60.85 6 ATOM 4171 CD1 LEU C 112 19.380 56.011 19.657 1.00 60.85 6 ATOM 4173 C LEU C 112 19.244 55.207 18.374 1.00 62.32 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4176 CA TYR C 113 23.943 55.389 21.429 1.00 53.49 18 ATOM 4176 CA TYR C 113 24.947 54.502 22.003 1.00 47.87 6 ATOM 4178 CG TYR C 113 24.947 54.502 22.003 1.00 47.87 6 ATOM 4180 CG1 TYR C 113 28.663 54.963 21.500 1.00 44.85 6 ATOM 4179 CD1 TYR C 113 28.663 54.963 22.502 1.00 40.84 6 ATOM 4180 CG1 TYR C 113 28.663 54.963 22.502 1.00 41.46 6 ATOM 4180 CG1 TYR C 113 28.663 54.963 23.138 1.00 40.68 6 ATOM 4180 CG1 TYR C 113 28.663 54.710 22.602 1.00 41.46 6 ATOM 4181 CD2 TYR C 113 28.663 54.710 22.602 1.00 41.46 6 ATOM 4180 CG1 TYR C 113 28.663 54.710 22.602 1.00 41.46 6 ATOM 4180 CG1 TYR C 113 28.663 54.710 22.502 27.79 1.00 39.26 6 ATOM 4180 CG1 TYR C 113 28.663 54.710 22.502 27.79 1.00 39.26 6 ATOM 4180 CG1 TYR C 113 28.663 54.710 22.502 27.79 1.00 40.68 6 ATOM 4180 CG1 TYR C 113 28.663 54.710 22.502 27.79 1.00 40.68 6 ATOM 4180 CG1 TYR C 113 28.663 54.710 22.502 27.79 1.00 40.68 6 ATOM 4180 CG1 TYR C 113 28.663 54.710 22.502 27.70 1.00 40.68 6 ATOM 4180 CG1 TYR C 113 28.663 54.710 22.502 27.70 1.00 40.68 6 ATOM 4180 CG1 TYR C 113 28.663 54.710 22.502 27.70 1.00 40.70 8 ATOM 4180 CG1 TYR C 113 28.663 54.710 22.502 27	20									1.00 59.61	
ATOM 4160 N VAL C 111 21.600 58.419 15.953 1.00 57.37 6 ATOM 4161 CA VAL C 111 22.444 57.379 16.535 1.00 55.43 6 ATOM 4162 CB VAL C 111 23.926 57.620 16.200 1.00 55.71 6 ATOM 4163 CGI VAL C 111 24.783 56.511 16.788 1.00 53.14 6 ATOM 4165 C VAL C 111 24.783 56.511 16.788 1.00 55.14 6 ATOM 4165 C VAL C 111 24.105 57.706 14.686 1.00 56.04 6 ATOM 4166 O VAL C 111 22.308 57.337 18.048 1.00 56.04 6 ATOM 4167 N LEU C 112 22.308 57.337 18.048 1.00 53.67 8 ATOM 4168 CA LEU C 112 22.050 55.992 20.034 1.00 53.67 8 ATOM 4169 CB LEU C 112 22.050 55.992 20.034 1.00 53.62 6 ATOM 4170 CG LEU C 112 20.638 55.548 20.420 1.00 55.64 6 ATOM 4171 CD1 LEU C 112 19.439 57.490 19.341 1.00 62.41 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4174 O LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4175 N TYR C 113 23.943 55.389 21.429 1.00 50.87 7 ATOM 4176 CA TYR C 113 24.947 54.502 22.003 1.00 47.87 6 ATOM 4178 CG TYR C 113 24.947 54.502 22.003 1.00 47.87 6 ATOM 4181 CD2 TYR C 113 26.362 54.924 21.560 1.00 44.85 6 ATOM 4181 CD2 TYR C 113 28.663 54.710 22.602 1.00 44.85 6 ATOM 4183 CZ TYR C 113 29.720 53.962 23.100 1.00 47.87 6 ATOM 4183 CZ TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4188 CA MET C 114 24.805 56.611 23.508 1.00 47.98 6 ATOM 4189 CB MET C 114 22.809 53.375 25.910 1.00 47.98 6 ATOM 4189 CB MET C 114 22.809 53.355 25.583 1.00 49.26 6 ATOM 4189 CB MET C 114 22.809 53.355 25.583 1.00 49.26 6 ATOM 4189 CB MET C 114 22.809 53.375 25.910 1.00 47.94 6 ATOM 4189 CB MET C 114 22.809 53.375 25.910 1.00 47.94 6 ATOM 4191 SD MET C 114 22.809 53.375 25.910 1.00 47.94 6 ATOM 4193 C MET C 114 22.809 53.375 25.910 1.00 47.94 6 ATOM 4193 C MET C 114 22.809 53.375 25.910 1.00 47.94 6 ATOM 4194 O MET C 114 22.805 55.2393 66.244 1.00 47.94 6 ATOM 4195 N MET C 114 22.805 55.2393 66.244 1.00 47.94 6 ATOM 4196 CD PRO C 115 27.207 51.556 27.066 1.00 48.95 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.95 6								56.995		1.00 60.95	
25 ATOM 4161 CA VAL C 111 23.926 57.620 16.200 1.00 55.71 6 ATOM 4163 CG1 VAL C 111 24.783 56.511 16.788 1.00 53.14 6 ATOM 4164 CG2 VAL C 111 24.783 56.511 16.788 1.00 55.04 6 ATOM 4165 C VAL C 111 24.783 56.511 16.788 1.00 55.04 6 ATOM 4166 C VAL C 111 22.308 57.337 18.048 1.00 54.63 6 ATOM 4166 N LEU C 111 22.328 58.373 18.706 1.00 53.67 8 ATOM 4167 N LEU C 112 22.050 55.992 20.034 1.00 53.62 6 ATOM 4169 CB LEU C 112 20.638 55.548 20.420 1.00 56.64 6 ATOM 4170 CG LEU C 112 19.439 57.490 19.341 1.00 62.41 6 ATOM 4171 CD1 LEU C 112 19.439 57.490 19.341 1.00 62.41 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4174 O LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4176 CA TYR C 113 23.943 55.389 21.429 1.00 53.087 7 ATOM 4176 CA TYR C 113 24.947 54.502 20.03 1.00 54.91 8 ATOM 4177 CB TYR C 113 26.362 54.924 21.560 1.00 44.85 6 ATOM 4180 CE1 TYR C 113 27.500 54.099 22.134 1.00 44.85 6 ATOM 4180 CE1 TYR C 113 28.663 54.710 22.602 1.00 44.85 6 ATOM 4181 CD2 TYR C 113 28.663 54.710 22.602 1.00 39.92 6 ATOM 4181 CD2 TYR C 113 28.663 54.710 22.602 1.00 39.92 6 ATOM 4185 C TYR C 113 29.625 52.583 23.138 1.00 41.66 6 ATOM 4186 C TYR C 113 29.625 52.583 23.138 1.00 40.07 8 ATOM 4186 C TYR C 113 29.625 52.583 23.138 1.00 40.68 6 ATOM 4186 C TYR C 113 24.457 53.508 24.146 1.00 40.88 7 ATOM 4186 C TYR C 113 29.625 52.583 23.138 1.00 40.70 8 ATOM 4186 C TYR C 113 29.625 52.583 23.138 1.00 40.68 6 ATOM 4187 N MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4188 C MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4193 N MET C 114 22.809 53.371 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 22.809 53.371 25.910 1.00 53.66 60 1.00 40.05 6 ATOM 4194 O MET C 114 22.805 55.277 27.696 1.00 65.99 6 ATOM 4196 CD PRO C 115 27.207 51.556 27.066 1.00 49.35 6 ATOM 4196 CD PRO C 115 27.207 51.556 27.066 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 49.35 6										1.00 57.63	
25 ATOM 4162 CB VAL C 111 23.926 57.620 16.207 1.00 53.14 6 ATOM 4164 CG2 VAL C 111 24.783 56.511 16.788 1.00 53.14 6 ATOM 4165 C VAL C 111 22.308 57.706 14.686 1.00 56.04 6 ATOM 4166 O VAL C 111 22.308 57.337 18.048 1.00 54.63 6 ATOM 4167 N LEU C 112 22.328 58.373 18.706 1.00 53.67 8 ATOM 4168 CA LEU C 112 22.050 55.992 20.034 1.00 53.62 6 ATOM 4169 CB LEU C 112 20.638 55.548 20.420 1.00 53.62 6 ATOM 4170 CD1 LEU C 112 19.380 56.011 19.657 1.00 60.85 6 ATOM 4171 CD1 LEU C 112 19.380 56.011 19.657 1.00 60.85 6 ATOM 4172 CD2 LEU C 112 19.380 56.011 19.657 1.00 62.32 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4175 N TYR C 113 23.024 53.807 20.134 1.00 54.91 8 ATOM 4176 CA TYR C 113 23.024 55.389 21.429 1.00 50.87 7 ATOM 4176 CA TYR C 113 24.947 54.502 22.003 1.00 47.87 6 ATOM 4180 CE1 TYR C 113 28.663 54.710 22.500 1.00 44.85 6 ATOM 4180 CE1 TYR C 113 28.663 54.710 22.500 1.00 44.85 6 ATOM 4180 CE2 TYR C 113 28.481 51.956 22.679 1.00 39.26 6 ATOM 4183 CZ TYR C 113 29.625 52.716 22.500 1.00 44.85 6 ATOM 4183 CZ TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4183 CZ TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4186 O TYR C 113 29.625 52.583 23.138 1.00 47.83 8 ATOM 4186 O TYR C 113 29.625 52.583 23.138 1.00 47.83 8 ATOM 4188 CA MET C 114 22.895 53.508 24.146 1.00 48.88 7 ATOM 4188 CA MET C 114 22.895 53.508 24.146 1.00 48.83 7 ATOM 4188 CA MET C 114 22.895 53.508 24.146 1.00 48.88 7 ATOM 4189 CB MET C 114 22.895 53.508 24.146 1.00 48.88 7 ATOM 4189 CB MET C 114 22.895 53.508 24.146 1.00 48.83 6 ATOM 4199 CB MET C 114 22.894 53.558 27.770 1.00 48.33 6 ATOM 4199 CB MET C 114 22.894 53.558 27.770 1.00 48.33 6 ATOM 4199 CB MET C 114 22.495 53.508 24.146 1.00 47.94 6 ATOM 4199 N MET C 114 22.494 55.556 27.766 1.00 49.35 6 ATOM 4199 N MET C 114 22.495 53.508 27.709 1.00 49.26 6 ATOM 4199 N MET C 114 22.495 53.508 27.709 1.00 49.35 6 ATOM 4199 N MET C 114 22.495 53.508 27.709 1.00 48.33 6 ATOM 4199 N MET C 114 22.495 53.556 27.706 1.00 49.35 6 ATOM 4199 N MET C 114 22.495 53.556 27.706 1.00 49.35										1.00 55.43	
ATOM 4163 CG1 VAL C 111	25										
ATOM 4165 C VAL C 111		ATOM	4163	CG1	VAL C 111	-					
ATOM 4166 O VAL C 111		MOTA								1.00 54.63	6
ATOM 4167 N LEU C 112 22.171 55.992 20.034 1.00 53.69 6 ATOM 4168 CA LEU C 112 22.050 55.992 20.034 1.00 53.66 6 6 ATOM 4169 CB LEU C 112 20.638 55.548 20.420 1.00 56.64 6 ATOM 4170 CG LEU C 112 19.380 56.011 19.657 1.00 60.85 6 ATOM 4171 CD1 LEU C 112 19.380 56.011 19.657 1.00 62.31 6 ATOM 4173 C LEU C 112 19.439 57.490 19.341 1.00 62.31 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4174 O LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4175 N TYR C 113 23.024 53.807 20.134 1.00 54.91 8 ATOM 4176 CA TYR C 113 24.947 54.502 22.003 1.00 47.87 6 ATOM 4177 CB TYR C 113 26.362 54.924 21.560 1.00 44.85 6 ATOM 4179 CD1 TYR C 113 27.500 54.099 22.134 1.00 40.84 6 ATOM 4180 CE1 TYR C 113 28.481 51.956 22.679 1.00 39.92 6 ATOM 4181 CD2 TYR C 113 28.481 51.956 22.679 1.00 39.92 6 ATOM 4181 CD2 TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4184 OH TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4184 OH TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4184 OH TYR C 113 29.720 53.962 23.100 1.00 40.78 8 ATOM 4184 OH TYR C 113 29.720 53.962 23.100 1.00 40.78 8 ATOM 4188 CA MET C 114 24.855 54.611 23.569 1.00 40.70 8 ATOM 4188 CA MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4190 CG MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4191 SD MET C 114 24.283 53.519 27.696 1.00 67.34 16 ATOM 4191 SD MET C 114 24.283 53.519 27.696 1.00 67.34 16 ATOM 4191 SD MET C 114 24.283 53.519 27.696 1.00 67.34 16 ATOM 4193 N MET C 114 24.485 51.360 27.7696 1.00 67.34 16 ATOM 4191 SD MET C 114 24.485 51.360 27.7696 1.00 67.34 16 ATOM 4193 N MET C 114 24.485 51.360 26.579 1.00 48.83 66 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.33 66 ATOM 4195 N MET C 114 24.485 51.360 26.579 1.00 48.35 66 ATOM 4195 N MET C 114 24.485 51.360 26.579 1.00 48.35 66 ATOM 4195 N MET C 114 24.485 51.360 26.579 1.00 48.35 66 ATOM 4195 N MET C 114 24.485 51.360 26.579 1.00 48.35 66 ATOM 4195 N MET C 114 24.485 51.360 26.579 1.00 48.35 66 ATOM 4195 N MET C 114 24.485 51.360 26.579 1.00 48.35 66 ATOM 4195 N MET C 114 24.485 51.360 26.579										1.00 53.67	
ATOM 4168 CA LEU C 112 22.050 55.992 20.034 1.00 53.62 6 ATOM 4169 CB LEU C 112 20.638 55.548 20.420 1.00 56.64 6 ATOM 4170 CG LEU C 112 19.380 56.011 19.657 1.00 60.85 6 ATOM 4171 CD1 LEU C 112 19.380 56.011 19.657 1.00 62.41 6 ATOM 4172 CD2 LEU C 112 19.439 57.490 19.341 1.00 62.41 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4174 O LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4175 N TYR C 113 23.943 55.389 21.429 1.00 50.87 7 ATOM 4176 CA TYR C 113 24.947 54.502 22.003 1.00 47.87 6 ATOM 4177 CB TYR C 113 26.362 54.924 21.560 1.00 44.85 6 ATOM 4179 CD1 TYR C 113 27.428 52.716 22.134 1.00 40.84 6 ATOM 4180 CE1 TYR C 113 28.481 51.956 22.679 1.00 39.26 6 ATOM 4181 CD2 TYR C 113 28.481 51.956 22.679 1.00 39.26 6 ATOM 4183 CZ TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4184 OH TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4185 C TYR C 113 24.457 53.508 1.00 40.70 8 ATOM 4186 O TYR C 113 29.625 55.673 24.089 1.00 40.70 8 ATOM 4186 O TYR C 113 24.457 53.508 1.00 40.70 8 ATOM 4186 O TYR C 113 24.457 53.508 1.00 40.70 8 ATOM 4187 N MET C 114 24.455 53.519 25.583 1.00 49.26 6 ATOM 4190 CG MET C 114 22.809 53.375 25.910 1.00 65.99 6 ATOM 4191 SD MET C 114 22.494 53.558 73.70 1.00 65.99 6 ATOM 4194 O MET C 114 22.494 53.558 73.70 1.00 65.99 6 ATOM 4195 N PRO C 115 26.364 52.927 7.696 1.00 47.40 7 ATOM 4195 N PRO C 115 26.364 52.927 7.696 1.00 47.40 7 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.30 66 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 26.364 52.927 7.696 1.00 49.35 6 ATOM 4196 CD PRO C 115 26.364 52.927 7.696 1.00 48.90 6	00				TRUC 11:	2			18.596		
ATOM 4169 CB LEU C 112 20.638 55.548 20.420 1.00 60.85 6 ATOM 4171 CD1 LEU C 112 19.380 56.011 19.657 1.00 60.85 6 ATOM 4171 CD1 LEU C 112 19.439 57.490 19.341 1.00 62.32 6 ATOM 4172 CD2 LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4173 C LEU C 112 23.024 53.807 20.134 1.00 54.91 8 ATOM 4175 N TYR C 113 23.943 55.389 21.429 1.00 50.87 7 ATOM 4176 CA TYR C 113 26.362 54.924 21.560 1.00 47.87 6 ATOM 4177 CB TYR C 113 26.362 54.924 21.560 1.00 44.85 6 ATOM 4179 CD1 TYR C 113 27.500 54.099 22.134 1.00 40.84 6 ATOM 4180 CE1 TYR C 113 28.481 51.956 22.679 1.00 39.26 6 ATOM 4183 CZ TYR C 113 28.663 54.710 22.602 1.00 41.11 6 ATOM 4183 CZ TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4185 C TYR C 113 24.805 54.611 23.508 1.00 40.70 8 ATOM 4186 O TYR C 113 24.805 54.611 23.508 1.00 40.70 8 ATOM 4188 CA TYR C 113 24.805 54.611 23.508 1.00 40.70 8 ATOM 4188 CA TYR C 113 24.805 54.611 23.508 1.00 49.26 6 ATOM 4189 CB MET C 114 24.457 53.508 27.370 1.00 55.99 6 ATOM 4190 CG MET C 114 22.809 53.375 25.910 1.00 55.99 6 ATOM 4191 SD MET C 114 22.809 53.375 25.910 1.00 55.99 6 ATOM 4191 SD MET C 114 22.809 54.330 27.098 1.00 65.99 6 ATOM 4193 C MET C 114 22.809 54.330 27.098 1.00 65.99 6 ATOM 4195 N PRO C 115 26.364 52.576 22.679 1.00 49.35 6 ATOM 4195 N PRO C 115 26.364 52.576 27.066 1.00 47.40 7 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 48.05 6 ATOM 4197 CA PRO C 115 27.181 53.711 25.976 1.00 48.05 6 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 48.05 6 ATOM 4197 CA PRO C 115 27.181 53.711 25.976 1.00 48.05 6 ATOM 4197 CA PRO C 115 27.181 53.711 25.976 1.00 48.05 6 ATOM 4197 CA PRO C 115 27.181 53.711 25.976 1.00 48.05 6 ATOM 4197 CA PRO C 115 27.181 53.711 25.976 1.00 48.05 6 ATOM 4197 CA PRO C 115 27.181 53.711 25.976 1.00 48.05 6	30						22.050			1.00 53.62	
ATOM 4170 CG LEU C 112 19.439 57.490 19.341 1.00 62.41 6 ATOM 4171 CD1 LEU C 112 19.439 57.490 20.542 1.00 53.28 6 ATOM 4173 C LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4174 O LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4175 N TYR C 113 23.943 55.389 21.429 1.00 50.87 7 ATOM 4176 CA TYR C 113 24.947 54.502 22.003 1.00 47.87 6 ATOM 4177 CB TYR C 113 26.362 54.924 21.560 1.00 44.85 6 ATOM 4178 CG TYR C 113 27.500 54.099 22.134 1.00 40.84 6 ATOM 4180 CE1 TYR C 113 27.428 52.716 22.181 1.00 39.92 6 ATOM 4181 CD2 TYR C 113 28.481 51.956 22.679 1.00 39.26 6 ATOM 4182 CE2 TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4184 OH TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4185 C TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4186 O TYR C 113 24.805 54.611 23.508 1.00 48.03 6 ATOM 4186 O TYR C 113 24.805 54.611 23.508 1.00 49.26 6 ATOM 4189 CB MET C 114 24.457 53.508 24.146 1.00 48.88 7 ATOM 4189 CB MET C 114 22.809 53.375 25.910 1.00 56.99 6 ATOM 4191 SD MET C 114 22.809 53.355 27.370 1.00 58.33 6 ATOM 4192 CE MET C 114 22.809 53.355 27.370 1.00 58.33 6 ATOM 4193 C MET C 114 22.809 53.355 27.370 1.00 58.33 6 ATOM 4194 O MET C 114 22.809 53.355 27.370 1.00 58.33 6 ATOM 4195 N MET C 114 22.809 53.355 27.370 1.00 58.33 6 ATOM 4193 C MET C 114 22.809 53.355 27.370 1.00 58.33 6 ATOM 4193 C MET C 114 22.809 53.355 27.370 1.00 58.33 6 ATOM 4193 C MET C 114 22.809 53.355 27.370 1.00 58.33 6 ATOM 4194 O MET C 114 22.809 53.355 27.370 1.00 58.33 6 ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6					LEU C 11	2				1.00 56.64	
ATOM											
ATOM 4172 CD2 LEU C 112 23.053 54.963 20.542 1.00 53.28 6 ATOM 4174 O LEU C 112 23.024 53.807 20.134 1.00 54.91 8 ATOM 4175 N TYR C 113 23.943 55.389 21.429 1.00 50.87 7 ATOM 4176 CA TYR C 113 24.947 54.502 22.003 1.00 47.87 6 ATOM 4177 CB TYR C 113 26.362 54.924 21.560 1.00 44.85 6 ATOM 4179 CD1 TYR C 113 27.500 54.099 22.134 1.00 40.84 6 ATOM 4180 CE1 TYR C 113 28.481 51.956 22.679 1.00 39.26 6 ATOM 4181 CD2 TYR C 113 28.663 54.710 22.602 1.00 41.11 6 ATOM 4181 CD2 TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4183 CZ TYR C 113 29.625 52.583 23.138 1.00 40.70 8 ATOM 4184 OH TYR C 113 29.625 52.583 23.138 1.00 40.70 8 ATOM 4185 C TYR C 113 24.805 54.611 23.508 1.00 48.03 6 ATOM 4186 O TYR C 113 24.805 54.611 23.508 1.00 48.88 7 6 ATOM 4189 CB MET C 114 24.855 55.002 55.673 24.089 1.00 47.83 8 ATOM 4189 CB MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4191 SD MET C 114 22.890 53.375 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 22.894 53.558 27.370 1.00 59.833 6 ATOM 4191 SD MET C 114 22.894 53.558 27.370 1.00 53.64 6 ATOM 4193 C MET C 114 22.894 53.558 27.370 1.00 53.64 6 ATOM 4193 C MET C 114 22.894 53.558 27.370 1.00 58.33 6 ATOM 4191 SD MET C 114 22.894 53.558 27.370 1.00 58.33 6 ATOM 4193 C MET C 114 22.894 53.558 27.370 1.00 58.33 6 ATOM 4194 O MET C 114 22.894 53.558 27.370 1.00 58.33 6 ATOM 4195 N PRO C 115 27.207 51.556 27.066 1.00 47.40 7 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 48.05 6 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 48.05 6 ATOM 4196 CD PRO C 115 27.207 51.556 27.066 1.00 48.05 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6			4171	CD1	LEU C 11	2				1.00 62.32	
ATOM 4174 O LEU C 112 23.024 53.807 20.134 1.00 54.91 8 ATOM 4175 N TYR C 113 23.943 55.389 21.429 1.00 50.87 7 ATOM 4176 CA TYR C 113 24.947 54.502 22.003 1.00 47.87 6 ATOM 4177 CB TYR C 113 26.362 54.924 21.560 1.00 44.85 6 ATOM 4179 CD1 TYR C 113 27.500 54.099 22.134 1.00 40.84 6 ATOM 4180 CE1 TYR C 113 27.428 52.716 22.181 1.00 39.92 6 ATOM 4181 CD2 TYR C 113 28.481 51.956 22.679 1.00 39.26 6 ATOM 4182 CE2 TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4183 CZ TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4184 OH TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4185 C TYR C 113 29.625 52.583 23.138 1.00 40.70 8 ATOM 4186 O TYR C 113 25.002 55.673 24.089 1.00 47.83 8 ATOM 4187 N MET C 114 24.805 54.611 23.508 1.00 48.03 6 ATOM 4188 CA MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4191 SD MET C 114 22.899 53.375 25.910 1.00 53.64 6 ATOM 4193 C MET C 114 22.899 53.375 25.910 1.00 53.64 6 ATOM 4193 C MET C 114 22.899 53.375 25.910 1.00 53.64 6 ATOM 4193 C MET C 114 22.899 53.375 25.910 1.00 53.64 6 ATOM 4195 N PRO C 115 22.494 53.558 27.370 1.00 58.33 6 ATOM 4195 N PRO C 115 22.494 53.556 26.440 1.00 47.94 6 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4196 CD PRO C 115 27.207 51.556 27.066 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 49.35 6	35	MOTA			LEU C 11	2				1.00 53.28	6
ATOM 4174					TEA C 11	2				1.00 54.91	
ATOM 4176 CA TYR C 113					TVR C 11	3				1.00 50.87	
40 ATOM 4177 CB TYR C 113 26.362 54.924 21.580 1.00 40.84 6 ATOM 4178 CG TYR C 113 27.500 54.099 22.134 1.00 40.84 6 ATOM 4179 CD1 TYR C 113 27.428 52.716 22.181 1.00 39.92 6 ATOM 4180 CE1 TYR C 113 28.663 54.710 22.602 1.00 41.11 6 ATOM 4181 CD2 TYR C 113 28.663 54.710 22.602 1.00 41.11 6 ATOM 4182 CE2 TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4183 CZ TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4184 OH TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4185 C TYR C 113 24.805 54.611 23.508 1.00 48.03 6 ATOM 4186 O TYR C 113 24.805 54.611 23.508 1.00 48.03 6 ATOM 4187 N MET C 114 24.805 55.673 24.089 1.00 47.83 8 ATOM 4188 CA MET C 114 24.283 53.519 25.583 1.00 48.88 7 ATOM 4189 CB MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4191 SD MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4193 C MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4193 C MET C 114 22.809 53.375 25.910 1.00 67.34 16 ATOM 4193 C MET C 114 22.809 53.375 25.910 1.00 67.34 16 ATOM 4193 C MET C 114 22.809 53.375 25.910 1.00 67.34 16 ATOM 4193 N PRO C 115 26.364 52.927 27.696 1.00 67.34 16 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6							24.947				
ATOM 4178 CG TYR C 113 27.500 54.099 22.134 1.00 39.92 6 ATOM 4179 CD1 TYR C 113 27.428 52.716 22.181 1.00 39.92 6 ATOM 4180 CE1 TYR C 113 28.481 51.956 22.679 1.00 39.26 6 ATOM 4181 CD2 TYR C 113 28.663 54.710 22.602 1.00 41.11 6 ATOM 4183 CZ TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4183 CZ TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4184 OH TYR C 113 30.667 51.831 23.649 1.00 40.70 8 ATOM 4185 C TYR C 113 24.805 54.611 23.508 1.00 48.03 6 ATOM 4186 O TYR C 113 25.002 55.673 24.089 1.00 47.83 8 ATOM 4187 N MET C 114 24.457 53.508 24.146 1.00 48.88 7 ATOM 4188 CA MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4190 CG MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4192 CE MET C 114 22.809 53.375 27.370 1.00 58.33 6 ATOM 4193 C MET C 114 22.809 53.375 27.098 1.00 67.34 16 ATOM 4194 O MET C 114 22.809 54.330 27.098 1.00 65.99 6 ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.94 6 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4196 CD PRO C 115 27.207 51.556 27.066 1.00 49.35 6	40				TYR C 11	.3					
ATOM 4180 CE1 TYR C 113 28.481 51.956 22.679 1.00 39.26 6 ATOM 4181 CD2 TYR C 113 28.663 54.710 22.602 1.00 41.11 6 ATOM 4181 CD2 TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4183 CZ TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4184 OH TYR C 113 30.667 51.831 23.649 1.00 40.70 8 ATOM 4185 C TYR C 113 24.805 54.611 23.508 1.00 48.03 6 ATOM 4186 O TYR C 113 25.002 55.673 24.089 1.00 47.83 8 ATOM 4187 N MET C 114 24.457 53.508 24.146 1.00 48.88 7 ATOM 4188 CA MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4190 CG MET C 114 22.899 53.375 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 22.494 53.558 27.370 1.00 58.33 6 ATOM 4192 CE MET C 114 22.494 53.558 27.370 1.00 58.33 6 ATOM 4193 C MET C 114 20.864 52.927 27.696 1.00 67.34 16 ATOM 4193 C MET C 114 25.055 52.393 26.244 1.00 47.94 6 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 ATOM 4196 CD PRO C 115 27.207 51.556 27.066 1.00 49.35 6	40			G CG	TYR C 11	.3					
ATOM 4181 CD2 TYR C 113 28.663 54.710 22.602 1.00 41.11 6 ATOM 4181 CD2 TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4183 CZ TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4184 OH TYR C 113 30.667 51.831 23.649 1.00 40.70 8 ATOM 4185 C TYR C 113 24.805 54.611 23.508 1.00 48.03 6 ATOM 4186 O TYR C 113 25.002 55.673 24.089 1.00 47.83 8 ATOM 4186 O TYR C 113 25.002 55.673 24.089 1.00 47.83 8 ATOM 4187 N MET C 114 24.457 53.508 24.146 1.00 48.88 7 ATOM 4188 CA MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4190 CG MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 22.494 53.558 27.370 1.00 58.33 6 ATOM 4192 CE MET C 114 20.864 52.927 27.696 1.00 67.34 16 ATOM 4193 C MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4196 CD PRO C 115 27.207 51.556 27.066 1.00 49.35 6			4179	CD1	TYR C 11	.3					
45 ATOM 4181 CD2 TYR C 113 29.720 53.962 23.100 1.00 40.68 6 ATOM 4182 CE2 TYR C 113 29.625 52.583 23.138 1.00 41.46 6 ATOM 4183 CZ TYR C 113 29.625 52.583 23.138 1.00 40.70 8 ATOM 4184 OH TYR C 113 24.805 54.611 23.508 1.00 48.03 6 ATOM 4185 C TYR C 113 24.805 54.611 23.508 1.00 48.03 6 ATOM 4186 O TYR C 113 25.002 55.673 24.089 1.00 47.83 8 ATOM 4187 N MET C 114 24.457 53.508 24.146 1.00 48.88 7 ATOM 4188 CA MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4190 CG MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 22.494 53.558 27.370 1.00 58.33 6 ATOM 4191 SD MET C 114 20.864 52.927 27.696 1.00 67.34 16 ATOM 4193 C MET C 114 20.864 52.927 27.696 1.00 65.99 6 ATOM 4193 C MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 49.35 6 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 49.35 6 6 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6		MOTA) CE	TYR C 11	.3					6
ATOM 4183 CZ TYR C 113					TYR C 11	.3 3				1.00 40.68	6
ATOM 4184 OH TYR C 113 30.667 51.831 23.649 1.00 40.70 8 ATOM 4185 C TYR C 113 24.805 54.611 23.508 1.00 48.03 6 ATOM 4186 O TYR C 113 25.002 55.673 24.089 1.00 47.83 8 ATOM 4187 N MET C 114 24.457 53.508 24.146 1.00 48.88 7 ATOM 4188 CA MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4189 CB MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4190 CG MET C 114 22.494 53.558 27.370 1.00 58.33 6 ATOM 4191 SD MET C 114 20.864 52.927 27.696 1.00 67.34 16 ATOM 4193 C MET C 114 25.055 52.393 26.244 1.00 47.94 6 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6	45				TYR C 13	.3				1.00 41.46	
ATOM 4185 C TYR C 113 24.805 54.611 23.508 1.00 47.83 8 ATOM 4186 O TYR C 113 25.002 55.673 24.089 1.00 47.83 8 ATOM 4187 N MET C 114 24.457 53.508 24.146 1.00 48.88 7 ATOM 4188 CA MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4189 CB MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4190 CG MET C 114 22.494 53.558 27.370 1.00 58.33 6 ATOM 4191 SD MET C 114 20.864 52.927 27.696 1.00 67.34 16 ATOM 4192 CE MET C 114 25.055 52.393 26.244 1.00 47.94 6 ATOM 4193 C MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6								51.831	23.649		
ATOM 4186 O TYR C 113 25.002 55.673 24.089 1.00 47.03 5 ATOM 4187 N MET C 114 24.457 53.508 24.146 1.00 48.88 7 ATOM 4188 CA MET C 114 24.283 53.519 25.583 1.00 49.26 6 ATOM 4189 CB MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 22.494 53.558 27.370 1.00 58.33 6 ATOM 4191 SD MET C 114 20.864 52.927 27.696 1.00 67.34 16 ATOM 4193 C MET C 114 19.859 54.330 27.098 1.00 65.99 6 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6					TYR C 1	13	24.805				
50 ATOM 4187 N MET C 114 24.457 53.508 24.146 1.00 49.26 6 ATOM 4188 CA MET C 114 22.809 53.519 25.583 1.00 49.26 6 ATOM 4190 CG MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4191 SD MET C 114 20.864 52.927 27.696 1.00 67.34 16 ATOM 4192 CE MET C 114 20.864 52.927 27.696 1.00 65.99 6 ATOM 4193 C MET C 114 25.055 52.393 26.244 1.00 47.94 6 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6					TYR C 1	13					
ATOM 4188 CA MET C 114 22.809 53.375 25.910 1.00 53.64 6 ATOM 4190 CG MET C 114 22.494 53.558 27.370 1.00 58.33 6 ATOM 4191 SD MET C 114 20.864 52.927 27.696 1.00 67.34 16 ATOM 4192 CE MET C 114 19.859 54.330 27.098 1.00 65.99 6 ATOM 4193 C MET C 114 25.055 52.393 26.244 1.00 47.94 6 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6	50				MET C 1	14					
ATOM 4189 CB MET C 114 22.494 53.558 27.370 1.00 58.33 6 27.404 4191 SD MET C 114 20.864 52.927 27.696 1.00 67.34 16 20.864 52.927 27.696 1.00 65.99 6 27.404 4193 C MET C 114 25.055 52.393 26.244 1.00 47.94 6 27.404 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 27.404 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 27.404 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 27.066 27.066 1.00 48.05 6 27.207 51.556 27.066 1.00 48.05 6 27.207 51.556 27.066 1.00 48.90 6				8 CA	MET C 1	14					
ATOM 4190 CG MET C 114 ATOM 4191 SD MET C 114 20.864 52.927 27.696 1.00 67.34 16 20.864 52.927 27.696 1.00 65.99 6 ATOM 4192 CE MET C 114 25.055 52.393 26.244 1.00 47.94 6 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 ATOM 4196 CD PRO C 115 ATOM 4197 CA PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6				_	MET C 1	14				1.00 58.33	6
55 ATOM 4191 SD MET C 114 19.859 54.330 27.098 1.00 65.99 6 ATOM 4192 CE MET C 114 25.055 52.393 26.244 1.00 47.94 6 ATOM 4193 C MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6										6 1.00 67.34	
ATOM 4193 C MET C 114 25.055 52.393 26.244 1.00 47.94 6 ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 48.32 8 ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6	E								_	8 1.00 65.99	
ATOM 4194 O MET C 114 24.485 51.360 26.579 1.00 47.40 7 ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6	55								-		
ATOM 4195 N PRO C 115 26.364 52.576 26.440 1.00 47.40 7 ATOM 4196 CD PRO C 115 27.181 53.711 25.976 1.00 49.35 6 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6					MET C 1	14					
ATOM 4196 CD PRO C 115 27.181 53.711 25.576 1.00 45.55 6 60 ATOM 4197 CA PRO C 115 27.207 51.556 27.066 1.00 48.05 6					PRO C 1	15					
60 ATOM 4197 CA PRO C 115 27.207 51.556 27.665 1.00 48.90 6		MOTA									_
ATOM 4198 CB PRO C 115 28.391 31.303 23.391	60	OTA (4 419							·	
		IOTA	M 419	98 CE	3 PRO C 1	.13	20.33				

PCT/EP01/01457

WO 01/58951

```
4199 CG PRO C 115 28.548 53.398 26.559 1.00 48.59
4200 C PRO C 115 27.153 51.636 28.585 1.00 48.68
4201 O PRO C 115 27.153 51.636 28.585 1.00 48.68
4201 N SER C 116 27.291 50.493 29.249 1.00 47.75
4202 N SER C 116 27.291 50.493 39.249 1.00 47.75
4203 CA SER C 116 27.291 50.493 39.249 1.00 47.75
4204 CB SER C 116 26.746 49.178 31.248 1.00 45.78
4205 CG SER C 116 28.743 50.607 31.097 1.00 47.39
4206 C SER C 116 28.743 50.607 31.097 1.00 47.39
4207 O SER C 116 29.568 49.794 30.695 1.00 48.39
4208 N LIE C 117 29.058 51.622 31.892 1.00 45.66
4209 CA LIE C 117 30.437 51.849 32.293 1.00 41.61
4211 CG2 LIE C 117 30.437 51.849 32.293 1.00 41.61
4211 CG2 LIE C 117 30.367 53.208 30.225 1.00 38.47
4212 CG1 LIE C 117 30.965 53.210 30.225 1.00 38.47
4213 CD1 LIE C 117 31.025 54.563 29.619 1.00 34.54
4214 C LIE C 117 30.078 51.830 33.796 1.00 42.87
4214 C LIE C 117 30.79 51.8189 31.230 1.00 34.54
4217 CA ARG C 118 31.787 51.158 34.182 1.00 40.75
4218 CB ARG C 118 33.277 48.558 34.182 1.00 40.75
4219 CG ARG C 118 33.277 48.558 38.156 1.00 42.87
4219 CG ARG C 118 33.874 48.693 38.453 1.00 40.35
4221 NE ARG C 118 33.874 48.693 38.453 1.00 39.40
4222 CZ ARG C 118 33.882 47.756 40.424 1.00 39.40
4224 NE ARG C 118 33.882 47.756 40.424 1.00 39.40
4224 NE ARG C 118 33.882 47.756 40.424 1.00 39.40
4229 CB GLN C 119 34.649 53.947 36.406 1.00 42.79
4220 CG ARG C 118 33.882 47.756 40.424 1.00 39.40
4221 NE ARG C 118 33.874 48.693 39.433 1.00 41.99
4222 CB GLN C 119 34.649 53.947 36.408 1.00 40.01
4236 CB ARG C 118 33.874 48.693 39.433 1.00 41.99
4230 CG GLN C 119 34.649 53.947 36.408 1.00 40.01
4237 CA ARG C 118 33.377 48.558 38.155 1.00 43.94
4224 NE ARG C 118 33.384 49.7556 40.424 1.00 39.40
4236 CG GLN C 119 35.506 59.39 35.034 1.00 44.99
4230 CG GLN C 119 35.506 59.39 37.31 1.00 41.00
4236 CB ARG C 120 37.355 53.696 40.397 1.00 45.00
4237 CA ARG C 118 33.396 46.574 40.208 1.00 40.01
4238 CB ARG C 120 37.355 53.696 40.397 1.00 45.00
4237 CA ARG C 120 37.355 53.696 40.397 1.00 45.00
4238 CB ARG C 120 37.355 53.696 40.397 1.00 46.89
424
                          ATOM
                          MOTA
                          MOTA
                          MOTA
                          MOTA
                          MOTA
                           MOTA
                           MOTA
                           MOTA
10
                            MOTA
                            MOTA
                            MOTA
                            MOTA
                             MOTA
15
                            MOTA
                              MOTA
                              MOTA
                              MOTA
                              MOTA
20
                              MOTA
                              MOTA
                              MOTA
                              MOTA
                               MOTA
  25
                               MOTA
                                MOTA
                                MOTA
                                MOTA
                                MOTA
   30
                                MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                  6
                                MOTA
                                MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                    6
                                 MOTA
                                 MOTA
   35
                                MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                    6
                                  MOTA
                                  MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                     7
                                  MOTA
                                  MOTA
      40
                                  MOTA
                                  MOTA
                                  MOTA
                                   MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                       6
                                    MOTA
       45
                                  MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                       7
                                    MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                       6
                                    MOTA
                                    MOTA
                                    MOTA
       50
                                    MOTA
                                     MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                        6
                                     MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                         6
                                     MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                         6
                                     MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                         6
         55
                                     MOTA
                                     MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                         6
                                       MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                          6
                                       MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                           8
                                       MOTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                         7
         60
                                       MOTA
                                        MOTA
```

PCT/EP01/01457

					-142				_
	MOTA	4260	CB .	SER C 122	38.799			1.00 51.31	6
	MOTA	4261		SER C 122	39.240		42.829	1.00 51.16	8
	MOTA	4262		SER C 122	36.387	63.213	42.365	1.00 50.12	6
	ATOM	4263		SER C 122	36.169	64.050	41.489	1.00 49.00	8
5	MOTA	4264		CYS C 123	35.687	63.156	43.488	1.00 50.55	7
3		4265		CYS C 123	34.636	64.112	43.754	1.00 52.50	6
	MOTA				34.356	64.198	45.246	1.00 54.52	6
	MOTA	4266		CYS C 123	34.998	63.514	46.043	1.00 54.24	8
	MOTA	4267		CYS C 123		63.709	42.993	1.00 53.16	6
	MOTA	4268		CYS C 123	33.377				16
10	MOTA	4269	SG	CYS C 123	32.811	62.031	43.374	1.00 56.86	7
	MOTA	4270	N	ASP C 124	33.389	65.037	45.622		6
	MOTA	4271	CA	ASP C 124	33.047	65.215	47.034	1.00 58.55	
	MOTA	4272	CB	ASP C 124	32.265	66.514	47.252	1.00 58.22	6
	MOTA	4273	CG	ASP C 124	32.506	67.105	48.634	1.00 58.91	6
15	MOTA	4274	OD1	ASP C 124	32.703	66.338	49.589	1.00 58.22	8
	MOTA	4275		ASP C 124	32.500	68.341	48.777	1.00 62.67	8
	MOTA	4276	C	ASP C 124	32.246	64.055	47.601	1.00 58.49	6
		4277	Ö	ASP C 124	31.098	63.837	47.229	1.00 58.26	8
	MOTA			VAL C 125	32.868	63.320	48.513	1.00 59.01	7
00	MOTA	4278	N		32.232	62.175	49.152	1.00 60.88	6
20	MOTA	4279	CA	VAL C 125		60.983	49.243	1.00 59.28	6
	MOTA	4280	CB.	VAL C 125	33.224		49.983	1.00 56.75	6
	MOTA	4281		VAL C 125	32.601	59.838		1.00 58.31	6
	MOTA	4282	CG2	VAL C 125	33.639	60.552	47.856	1.00 63.26	6
	MOTA	4283	С	VAL C 125	31.740	62.530	50.565		8
25	MOTA	4284	0	VAL C 125	30.892	61.833	51.143	1.00 63.90	7
	MOTA	4285	N	SER C 126	32.267	63.616	51.122	1.00 63.98	
	MOTA	4286	CA	SER C 126	31.878	64.026	52.464	1.00 64.49	6
	MOTA	4287	CB	SER C 126	32.464	65.400	52.793	1.00 63.93	6
		4288	OG	SER C 126	31.972	66.381	51.898	1.00 61.34	8
20	MOTA	4289	C	SER C 126	30.364	64.061	52.614	1.00 64.90	6
30	MOTA			SER C 126	29.654	64.603	51.766	1.00 64.08	8
	MOTA	4290	0	GLY C 127	29.871	63.458	53.689	1.00 66.05	7
	MOTA	4291	N		28.442	63.458	53.929	1.00 68.25	6
	MOTA	4292	CA	GLY C 127	27.742	62.201	53.467	1.00 69.88	6
	MOTA	4293	С	GLY C 127			53.679	1.00 70.57	8
35	MOTA	4294	0	GLY C 127	26.546	62.040	52.839	1.00 71.23	7
	MOTA	4295	N	VAL C 128	28.480	61.297		1.00 72.78	6
	ATOM	4296	CA	VAL C 128	27.871	60.065	52.366	1.00 72.70	6
	MOTA	4297	CB	VAL C 128	28.890	59.124	51.690		6
	MOTA	4298	CG1	VAL C 128	29.282	59.670	50.361	1.00 75.47	6
40	ATOM	4299		VAL C 128	30.104	58.940	52.585	1.00 70.24	
-10	MOTA	4300		VAL C 128	27.223	59.242	53.466	1.00 74.00	6
	MOTA	4301		VAL C 128	26.090	58.770	53.316	1.00 73.73	8
	MOTA	4302		ASP C 129	27.946	59.063	54.567	1.00 75.39	7
		4303		ASP C 129	27.440	58.222	55.628	1.00 77.33	6
ΛE	MOTA	4304		ASP C 129	28.490		56.721	1.00 77.51	6
45	MOTA			ASP C 129	28.304		57.486	1.00 78.34	6
	MOTA	4305			29.328		57.770	1.00 78.50	8
	MOTA	4306		1 ASP C 129	27.132		57.803	1.00 77.23	8
	MOTA	4307		2 ASP C 129			56.235		6
	MOTA	4308	3 C	ASP C 129	26.114		56.948		8
50	MOTA	4309	9 0	ASP C 129	25.497				7
	MOTA	4310) N	THR C 130	25.645		55.948		6
	MOTA	4313	L CA		24.365		56.521		
	MOTA	4312	2 CB	THR C 130	24.447		58.077		6
	MOTA	431		1 THR C 130	25.829		58.472		8
55		431			23.618		58.670		6
55	ATOM	431		THR C 130	23.705	61.566	56.146	1.00 79.50	6
	ATOM			THR C 130	24.362		55.760		8
				GLU C 131	22.382		56.307		7
	MOTA				21.48			1.00 79.61	6
	MOTA				21.98			1.00 82.70	6
60					21.68				6
	MOTA	432	0 CG	9 GTO C TOT	21.00				

-142

PCT/EP01/01457 WO 01/58951

```
MOTA
  MOTA
  MOTA
  MOTA
  MOTA
  MOTA
  MOTA
  MOTA
  MOTA
10
15
20
25
30
35
40 ATOM
45
 50 ATOM
 55
 60
```

PCT/EP01/01457

						-144				
	3 mov	4300	NT T	LE C 140			65.761	32.036	1.00 51.29	7
	MOTA ATOM	4382 4383		LE C 140				30.842	1.00 50.15	6
	ATOM	4384		LE C 140		31.404	63.613	30.769	1.00 51.22	6
	ATOM	4385		LE C 140		31.536	62.955	32.134	1.00 52.05	6
5	MOTA	4386		LE C 140		29.930	63.555	30.393	1.00 49.11	6
	MOTA	4387	CD1	LE C 140		29.307	62.187	30.676	1.00 49.89	6
	MOTA	4388		LE C 140		31.624	65.861	29.560	1.00 47.99	6 8
	MOTA	4389		TLE C 140		30.515	66.323	29.365 28.701	1.00 50.04 1.00 46.57	7
4.0	MOTA	4390		3LY C 141		32.620 32.414	66.025 66.732	27.447	1.00 46.87	6
10	MOTA	4391		GLY C 141 GLY C 141		33.453	66.323	26.416	1.00 46.66	6
	MOTA	4392 4393		GLY C 141		34.359	65.565	26.739	1.00 46.42	8
	MOTA MOTA	4394		SER C 142		33.329	66.804	25.180	1.00 45.19	7
	MOTA	4395		SER C 142		34.303	66.474	24.140	1.00 41.98	6
15	ATOM	4396		SER C 142		33.974	67.165	22.828	1.00 40.96	6
	ATOM	4397	OG	SER C 142		35.062	67.057	21.943	1.00 34.78	8
	MOTA	4398		SER C 142		35.698	66.885	24.551	1.00 43.33 1.00 45.01	6 8
	MOTA	4399		SER C 142		35.915	67.956	25.115 24.256	1.00 43.01	7
	MOTA	4400		TRP C 143		36.655	66.028 66.300	24.230	1.00 43.12	6
20	MOTA	4401		TRP C 143		38.025 38.768	64.982	24.819	1.00 41.57	6
	MOTA	4402		TRP C 143 TRP C 143		40.125	65.141	25.446	1.00 39.54	6
	MOTA	4403 4404		TRP C 143		40.394	65.420	26.820	1.00 36.50	6
	MOTA MOTA	4405		TRP C 143		41.795	65.481	26.967	1.00 35.30	6
25	ATOM	4406		TRP C 143		39.584	65.625	27.943	1.00 36.55	6
20	MOTA	4407		TRP C 143		41.345	65.048	24.829	1.00 38.96	6
	MOTA	4408	NE1	TRP C 143		42.353	65.251	25.738	1.00 35.00	7 6
	MOTA	4409		TRP C 143		42.400	65.736	28.192	1.00 34.47 1.00 35.28	6
•	MOTA	4410		TRP C 143		40.185	65.878	29.153 29.271	1.00 35.26	6
30	ATOM	4411		TRP C 143		41.580	65.931 67.159	23.605	1.00 43.69	6
	MOTA	4412	C	TRP C 143		38.767 39.657	67.135	23.962	1.00 46.65	8
	MOTA	4413	O	TRP C 143		38.402	67.065	22.338	1.00 42.21	7
	MOTA	4414 4415	N CA	THR C 144		39.107	67.834	21.333	1.00 40.90	6
35	MOTA MOTA	4416	CB	THR C 144		39.839	66.901	20.372	1.00 40.06	6
00	MOTA	4417	OG1			38.907	65.976	19.798	1.00 40.17	8
	MOTA	4418	CG2			40.916	66.144	21.106	1.00 38.34	6
	MOTA	4419	С	THR C 144		38.252	68.795	20.520	1.00 43.03 1.00 43.02	6 8
	MOTA	4420	0	THR C 144		38.786	69.631	19.795	1.00 43.02	7
40	MOTA	4421	N	HIS C 145		36.934	68.687 69.571	20.635 19.885	1.00 45.42	6
	MOTA	4422	CA	HIS C 145) -	36.065 34.994	68,772	19.144	1.00 48.25	6
	MOTA	4423		HIS C 145		35.533	67.873	18.071	1.00 49.32	6
	MOTA	4424 4425	CD3	HIS C 14		36.052	68.154	16.853	1.00 47.20	6
45	MOTA MOTA	4426		HIS C 14		35.572	66.500	18.197	1.00 47.13	7
45	MOTA	4427	CE1	HIS C 14	5	36.091	65.976	17.103	1.00 47.99	6
	MOTA	4428	NE2	HIS C 14	5	36.391	66.958	16.272	1.00 48.34	7
	MOTA	4429		HIS C 14	5	35.394	70.627	20.754		6 8
	MOTA	4430	0	HIS C 14	5	34.738	70.325	21.746		7
50	MOTA	4431		HIS C 14	6	35.562	71.883 72.993	20.363 21.094		6
	MOTA	4432		HIS C 14		34.972 35.777		20.840		6
	MOTA	4433		HIS C 14 HIS C 14		35.777		19.390		6
	MOTA	4434	G CG	HIS C 14	6	35.013		18.409		6
55	MOTA	4435 4436		HIS C 14	6	37.161		18.801	1.00 48.82	7
55	MOTA MOTA	443		HIS C 14		36.993		17.519	1.00 48.32	6
	MOTA	443		HIS C 14	6	35.699	75.043			7
	ATOM	443		HIS C 14	6	33.524				6
	MOTA	444		HIS C 14	6	33.047				8 7
60				SER C 14		32.847				6
	MOTA	444	2 CA	SER C 14	7	31.437	74.418	21.115	, 1.00 57.25	-

						1.45				
						-145 31.055	75.610	21.978	1.00 57.36	6
	MOTA			ER C 14		32.017	76.635	21.828	1.00 59.18	8
	MOTA			ER C 14		30.972	74.660	19.682	1.00 57.72	6
	MOTA		-	ER C 14		29.790	74.484	19.375	1.00 57.25	8
5	MOTA MOTA			RG C 14		31.885	75.065	18.809	1.00 58.23	7
3	MOTA			RG C 14		31.517	75.336	17.424	1.00 60.12	6
	MOTA			RG C 14		32.555	76.264	16.777	1.00 63.75	6 6
	ATOM	4450		RG C 1		32.799	77.567	17.549	1.00 70.83 1.00 77.31	6
	MOTA	4451	CD A	RG C 1	48	33.950	78.393	16.946	1.00 77.31	7
10	MOTA	4452		RG C 1		34.422	79.453	17.852 18.245	1.00 84.13	6
	MOTA	4453		RG C 1		33.696	80.506	18.245	1.00 87.64	7
	MOTA	4454	NH1 A	RG C 1	48	32.447	80.661 81.408	19.072	1.00 86.26	7
	ATOM	4455	NH2 A	RG C 1	48	34.213 31.390	74.051	16.601	1.00 59.83	6
	MOTA	4456		RG C 1		30.786	74.051	15.519	1.00 60.30	8
15	MOTA	4457		RG C 1		31.954	72.959	17.121	1.00 57.69	7
	MOTA	4458	N G	LU C 1	49	31.937	71.677	16.425	1.00 54.67	6
	MOTA	4459	CA G	LUCI	49	33.364	71.132	16.321	1.00 52.47	6
	MOTA	4460		LU C 1		34.395	72.228	16.050	1.00 52.11	6
20	MOTA	4461 4462	CD G	ELU C 1	49	35.824	71.718	15.896	1.00 50.20	6
20	MOTA MOTA	4463	OE1 G	ELU C 1	49	36.246	70.852	16.678	1.00 49.43	8
	MOTA	4464	OE2	LU C 1	49	36.537	72.203	15.004	1.00 47.62	8 6
	MOTA	4465		ELU C 1		31.043	70.698	17.162	1.00 53.64	8
	MOTA	4466	0 (GLU C 1	L49	30.252		16.552	1.00 53.16 1.00 52.16	7
25	MOTA	4467	N	ILE C	150	31.172		18.479	1.00 52.10	6
	MOTA	4468		ILE C		30.353		19.289 19.883	1.00 53.49	6
	MOTA	4469	CB :	ILE C	150	31.157			1.00 52.00	6
	MOTA	4470	CG2	ILE C	150	30.361			1.00 53.48	6
	MOTA	4471		ILE C		31.450 32.235			1.00 50.44	6
30	MOTA	4472		ILE C	150	29.750			1.00 53.26	6
	MOTA	4473		ILE C		30.410			1.00 51.01	8
	MOTA	4474		SER C		28.479			1.00 54.99	7
	MOTA	4475	N CA	SER C	151	27.749			1.00 56.94	6
25	MOTA	4476 4477	CB	SER C	151	26.693	3 71.873			6 8
35	MOTA MOTA	4478	OG	SER C	151	25.66				6
	MOTA	4479	C	SER C	151	27.08				8
	MOTA	4480	Ō	SER C	151	26.53				7
	MOTA	4481	N	VAL C	152	27.17				6
40	ATOM	4482	CA	VAL C	152	26.56				
	MOTA	4483	СВ	VAL C	152	27.56				6
	MOTA	4484	CG1	VAL C	152	28.85 27.81				6
	MOTA			VAL C	152	25.37				6
	MOTA			VAL C	152	25.37			3 1.00 63.73	. 8
45	MOTA			VAL C ASP C		24.34			1 1.00 65.81	. 7
	MOTA			ASP C	153	23.14		7 26.29	3 1.00 67.23	6
	MOTA			ASP C		22.15				6
	MOTA			ASP C	153	22.74				3 6
50	MOTA MOTA (_		ASP C	153	22.78				8 L 8
50	MOTA		OD2	ASP C	153	23.19			11	6
	ATOM			ASP C	153	22.50				
	ATOM			ASP C	153	22.50				97
	MOTA			PRO C	154	21.9				
55			7 CD	PRO C	154	22.2				8 6
	MOTA			PRO C	154	21.3 21.1		·		4 6
	MOTA			PRO C		22.3			3 1.00 71.3	5 6
	OTA			PRO C	. 154	19.9			2 1.00 77.2	5 6
~	OTA			PRO (, 154 , 154	19.5			32 1. 00 77.7	6 8
6				THR (155	19.2	_			7 7
	OTA	м 450	3 N	7.11.		_				

PCT/EP01/01457

						-140				_
	MOTA	4504	CA	THR C 155		18.010	65.253	28.633	1.00 83.84	6
	MOTA	4505		THR C 155		18.244	63.932	27.837	1.00 83.53	6
	ATOM	4506		THR C 155		18.609	62.882	28.744	1.00 83.26	8
	ATOM	4507		THR C 155		19.361	64.105	26.823	1.00 83.08	6
5	ATOM	4508		THR C 155		16.897	65.001	29.678	1.00 87.74	6
J	MOTA	4509	ō	THR C 155		16.826	65.677	30.715	1.00 87.94	8
	MOTA	4510	N	THR C 156		16.042	64.012	29.370	1.00 91.72	7
	MOTA	4511	CA	THR C 156		14.882	63.577	30.180	1.00 93.73	6
		4512	CB	THR C 156		14.501	62.092	29.877	1.00 93.94	6
10	MOTA MOTA	4513	OG1	THR C 156		14.249	61.933	28.470	1.00 93.93	8
10		4514	CG2	THR C 156		13.253	61,681	30.696	1.00 93.29	6
	MOTA		C	THR C 156		15.042	63.695	31.693	1.00 95.32	6
	ATOM	4515		THR C 156		15.626	62.817	32.347	1.00 95.61	8
	MOTA	4516	0	GLU C 157		14.490	64.767	32.246	1.00 97.07	7
4 =	MOTA	4517	N	GLU C 157		14.578	65.011	33.679	1.00 98.94	6
15	MOTA	4518	CA			14.487	66.514	33.942	1.00100.27	6
	MOTA	4519	CB	GLU C 157		15.282	67.359	32.950	1.00102.55	6
	MOTA	4520	CG	GLU C 157		15.113	68.852	33.214	1.00104.54	6
	MOTA	4521	CD	GLU C 157		13.943	69.322	33.312	1.00105.88	8
	MOTA	4522	OE1	GLU C 157		16.150	69.555	33.327	1.00104.90	8
20	MOTA	4523	OE2	GLU C 157			64.290	34.465	1.00 99.30	6
	MOTA	4524	С	GLU C 157		13.475	64.337	35.706	1.00 99.77	8
	MOTA	4525	0	GLU C 157		13.452	63.639	33.751	1.00 99.15	7
	MOTA	4526	N	ASN C 158		12.557		34.404	1.00 98.32	6
	MOTA	4527	CA	ASN C 158		11.457	62.919 62.541	33.374	1.00100.43	6
25	MOTA	4528	CB	ASN C 158		10.382		32.555	1.00101.38	6
	MOTA	4529	CG	ASN C 158		9.902	63.736	33.112	1.00101.96	8
	MOTA	4530	OD1			9.423	64.738	31.224	1.00101.30	7
	MOTA	4531	ND2			10.026	63.636	35.064	1.00 96.64	6
	MOTA	4532	С	ASN C 158		11.991	61.638	36.239	1.00 96.33	8
30	MOTA	4533	0	ASN C 158		12.380	61.643		1.00 93.61	7
	MOTA	4534	N	SER C 159		11.992	60.558	34.283	1.00 90.35	6
	MOTA	4535	CA	SER C 1:59		12.466	59.237	34.690	1.00 90.84	6
	MOTA	4536	CB	SER C 159		13.541	58.788	33.690	1.00 90.44	8
	MOTA	4537	OG	SER C 159	1	14.367	59.898	33.320	1.00 90.44	6
35	MOTA	4538	С	SER C 159		13.005	59.167	36,123	1.00 88.99	8
	MOTA	4539	0	SER C 159)	13.942	59.894	36.481	1.00 84.53	7
	MOTA	4540	N	ASP C 160		12.414	58.302	36.945	1.00 84.33	6
	ATOM	4541	CA	ASP C 160		12.863	58.152	38.330	1.00 80.47	б
	ATOM	4542	CB	ASP C 160		12.232	56.921	38.985	1.00 80.20	6
40	MOTA	4543	CG	ASP C 160		12.760	56.683	40.398	1.00 82.12	8
	MOTA	4544		L ASP C 160)	12.658	55.536	40.890	1.00 82.78	8
	MOTA	4545	OD	2 ASP C 160)	13.277	57.644	41.023	1.00 82.17	6
	MOTA	4546	С	ASP C 16		14.380	57.978	38.340	1.00 77.39	8
	MOTA	4547	0	ASP C 16		14.892	57.009	37.768		7
45	MOTA	4548	N	ASP C 16		15.080	58.910	38.992		6
	ATOM	4549	CA	ASP C 16	L	16.529	58.864	39.072	1.00 71.77	
	MOTA	. 4550		ASP C 16	L	17.060	59.934	40.028	1.00 71.93	6
	MOTA	4551			1	16.943	61.330			6
	MOTA	4552		1 ASP C 16	1	17.115	61.486	38.230		8
50	MOTA	4553		2 ASP C 16	1	16.695	62.270	40.246		8
00	ATOM	4554		ASP C 16	1	17.118	57.515	39.479	1.00 70.97	6
	MOTA			ASP C 16	1	18.296	57.251			8
	MOTA	4556		SER C 16	2	16.335	56.649			7
	MOTA					16.899		40.496		6
55	MOTA				2	17.085		42.020		6
55	MOTA					15.845		42.698	1.00 66.84	8
	MOTA			SER C 16	2	16.064		40.019		6
	ATOM			SER C 16	2	16.042				8
	ATOM			GLU C 16	3	15.393		38.892		7
60					3	14.571		38.398		6
00	ATOM					13.543		37.372	2 1.00 68.86	6
	AIOM	4.50							•	

PCT/EP01/01457

						-147				_
	MOTA	4565	CG G	LU C 163		14.029			1.00 70.35	6
	MOTA	4566		LU C 163		12.886			1.00 73.03	6
	ATOM	4567		LU C 163		12.345	55.390	35.065	1.00 75.39	8
	ATOM	4568		LU C 163		12.517	53.378	34.193	1.00 72.63	8
5	MOTA	4569		LU C 163		15.416	52.145	37.808	1.00 65.46	6
5				LU C 163		14.902	51.071	37.481	1.00 64.98	8
	MOTA	4570		YR C 164		16.718	52.392	37.675	1.00 65.54	7
	MOTA	4571				17.647	51.389	37.143	1.00 63.20	6
	MOTA	4572		YR C 164		18.353	51.894	35.884	1.00 63.41	6
	MOTA	4573		YR C 164				34.716	1.00 65.49	6
10	MOTA	4574		YR C 164		17.433	52.101		1.00 66.61	6
	MOTA	4575		YR C 164		17.299	53.355	34.119	1.00 68.54	6
	MOTA	4576		TYR C 164		16.429	53.555	33.046	1.00 60.34	6
	MOTA	4577	CD2 T	TYR C 164		16.676	51.046	34.216	1.00 68.25	
	MOTA	4578	CE2 T	YR C 164		15.797	51.230	33.144	1.00 70.31	6
15	MOTA	4579	CZ 7	TYR C 164		15.680	52.484	32.562	1.00 70.26	6
10	MOTA	4580		TYR C 164		14.832	52.655	31.482	1.00 74.21	8
		4581	C 7	TYR C 164		18.690	51.066	38.184	1.00 61.13	6
	MOTA			TYR C 164		19.480	50.147	38.003	1.00 60.53	8
	MOTA	4582		PHE C 165		18.687	51.824	39.279	1.00 59.92	7
-00	ATOM	4583				19.657	51.622	40.347	1.00 58.58	6
20	MOTA	4584		PHE C 165		19.497	52.690	41.425	1.00 56.39	6
	MOTA	4585		PHE C 165				42.288	1.00 55.60	6
	MOTA	4586		PHE C 165		20.717	52.856	41.742	1.00 53.27	6
	MOTA	4587	CD1	PHE C 165		21.904	53.336		1.00 54.20	6
	MOTA	4588		PHE C 165		20.692	52.497	43.629	1.00 54.20	6
25	ATOM	4589	CE1	PHE C 165		23.049	53.451	42.513		6
	ATOM	4590	CE2	PHE C 165		21.835	52.607	44.414	1.00 54.70	
	MOTA	4591	CZ	PHE C 165		23.018	53.085	43.854	1.00 54.90	6
	MOTA	4592		PHE C 165		19.528	50.250	40.974	1.00 58.64	6
		4593		PHE C 165		18.422	49.749	41.153	1.00 60.35	8
20	MOTA			SER C 166		20.655	49.631	41.298	1.00 58.50	7
30	MOTA	4594		SER C 166		20.614	48.309	41.900	1.00 58.50	6
	MOTA	4595		SER C 166		22.013	47.703	41.996	1.00 58.83	6
	MOTA	4596	CB			21.957	46.391	42.542	1.00 61.34	8
	MOTA	4597	OG	SER C 166		20.050	48.473	43.286	1.00 58.49	6
	MOTA	4598	С	SER C 166			49.454	43.964	1.00 58.40	8
35	MOTA	4599	0	SER C 166		20.346		43.706	1.00 57.37	· 7
	ATOM	4600	N	GLN C 16'		19.249	47.503	45.020	1.00 57.17	6
	MOTA	4601	CA	GLN C 16'		18.631	47.545		1.00 59.70	6
	MOTA	4602	CB	GLN C 16.		17.317		44.994	1.00 62.90	6
	MOTA	4603	CG	GLN C 16	7	17.467		44.490	1.00 02.30	6
40	MOTA	4604		GLN C 16	7	16.136		44.164	1.00 67.19	8
70	MOTA	4605		GLN C 16	7	15.284	44.519	45.048	1.00 68.37	
•	MOTA	4606				15.940	44.334	42.884	1.00 66.77	7
		4607		GLN C 16		19.548	46.975	46.085	1.00 55.30	6
	MOTA	4608		GLN C 16		19.373	47.235	47.271	1.00 53.36	8
4.5	MOTA	4609		TYR C 16		20.541		45.659	1.00 55.00	7
45	MOTA			TYR C 16		21.455		46.609	1.00 55.48	6
	MOTA	4610				21.845			1.00 55.25	6
	MOTA	4611		TYR C 16		20.630				6
	MOTA	4612	2 CG	TYR C 16	8	20.030			00	6
	MOTA	4613	3 CD1	TYR C 16	8					6
50	MOTA	4614	4 CE1	TYR C 16	8	19.087				6
	MOTA	461	5 CD2	TYR C 16	8	19.825				6
	ATOM	461	6 CE2	TYR C 16	8	18.664				
	MOTA			TYR C 16	8	18.300			1.00 58.82	6
	MOTA			TYR C 16	8	17.13				8
55				TYR C 1		22.69				6
55				TYR C 16	8	23.58		7 47.637	1.00 53.34	8
	MOTA			SER C 1	59	22.73				7
	ATOM			SER C 1	59	23.85				6
	ATOM			SEV C I	59	23.73		_	1.00 58.39	6
	MOTA			SER C 1	50	24.74				
60				SER C 1	60	23.86				
	MOTA	462	5 C	SER C 1	צס	23.80	U 49.00.		-	

PCT/EP01/01457

					-148				
	MOTA	4626	O SER	C 169	22.803	49.148		1.00 60.78	
	MOTA		N ARG		25.052	49.215	48.621	1.00 59.44	4 7
	ATOM			C 170	25.174	49.662	49.998	1.00 58.3	9 6
	MOTA			C 170	26.636	49.602	50.438	1.00 59.1	
5	ATOM	4630		C 170	26.999	48.350	51.195	1.00 61.6	
J	MOTA	4631		C 170	28.466	47.972	51.024	1.00 64.8	
	MOTA	4632		C 170	29.418	49.012	51.424	1.00 66.4	
	MOTA	4633		C 170	30.317	49.556	50.597	1.00 68.2	8 6
	MOTA	4634		C 170	30.384	49.165	49.326	1.00 66.2	
10	MOTA	4635	NH2 ARG	C 170	31.166	50.480	51.039	1.00 68.6	
10	MOTA	4636	C ARG	C 170	24.668	51.102	50.109	1.00 59.2	
		4637	O ARG		24.416	51.609	51.215	1.00 59.9	9 8
	MOTA	4638		C 171	24.498	51.759	48.968	1.00 57.0	
	MOTA	4639		C 171	24.063	53.146	48.982	1.00 56.4	
15	MOTA		CB PHE	C 171	25.131	54.016	48.324	1.00 55.2	
15	ATOM	4640		C 171	26.521	53.719	48.814	1.00 54.5	61 6
	MOTA	4641	CD1 PH		27.189	52.568	48.400	1.00 55.9	8 6
	MOTA	4642		C 171	27.145	54.559	49.724	1.00.53.2	
	MOTA	4643		E C 171	28.463	52.257	48.890	1.00 55.0	9 6
00	MOTA	4644		E C 171	28.412	54.258	50.218	1.00 54.2	
20	MOTA	4645		E C 171	29.074	53.102	49.799	1.00 54.8	
	MOTA	4646			22.732	53.346	48.311	1.00 55.7	77 6
	MOTA	4647	_		22.164	52.406	47.761	1.00 55.	57 8
	MOTA	4648		E C 171 U C 172	22.228	54.569	48.376	1.00 55.3	26 7
	MOTA	4649			20.947	54.877	47.760	1.00 58.	65 6
25	MOTA	4650	CA GL	U C 172	19.806	54.769	48.789	1.00 60.	96 6
	MOTA	4651		U C 172	19.891	55.739	49.981	1.00 64.	19 6
	MOTA	4652		U C 172	18.753	55.551	50.992	1.00 64.	82 6
	MOTA	4653		U C 172	17.626	55.236	50.557	1.00 65.	38 8
	MOTA	4654	OE1 GL	U C 172	18.976	55.734	52.216	1.00 64.	87 8
30	MOTA	4655		υ C 172	21.014	56.279	47.162	1.00 59.	71 6
	MOTA	4656		υ C 172	21.014		47.600	1.00 60.	
	MOTA	4657	O GI	υ C 172		56.530	46.154	1.00 58.	
	MOTA	4658		E C 173	20.186 20.182			1.00 59.	
	MOTA	4659		E C 173	20.182			1.00 60.	
35	MOTA	4660		SE C 173	19.918			1.00 57.	
	MOTA	4661	CG2 II	LE C 173				1.00 59.	
	MOTA	4662	CG1 II	LE C 173	21.191 21.053			1.00 58	
	MOTA	4663		LE C 173	19.088			1.00 59	. 99 6
	MOTA	4664		LE C 173	17.912				.81 8
40	MOTA	4665	O I	LE C 173	19.480				. 93 7
	MOTA	4666		EU C 174					
	MOTA	4667		EU C 174	18.510 19.164				
	MOTA	4668		EU C 174	19.164	_			.64 6
	MOTA	4669	CG L	EU C 174					.25 6
45	MOTA	4670) CD1 L	EU C 174	20.64				
	MOTA	4671	CD2 L	EU C 174	19.05				
	MOTA	4672	S C P	EU C 174	17.98				.71 8
	MOTA	4673	30 L	EU C 174	16.78				.23 7
	MOTA	4674	1 N A	SP C 175	18.89		1 43.576		
50	MOTA	467	5 CA A	SP C 175	18.48				.24 6
	MOTA	467	6 CB A	SP C 175	17.94	_			
	MOTA		7 CG A	ASP C 175	17.41				
	ATOM		8 OD1 F	ASP C 175	16.59	8 64.65	-		5.59 8
	MOTA	467	9 OD2 F	ASP C 175	17.81				
55			0 C 1	ASP C 175	19.65	1 63.08	-		
	ATOM		1 0 7	ASP C 175	20.82				
	MOTA		2 N 7	VAL C 176	19.31				
	MOTA		3 CA 1	VAL C 176	20.30				
	ATOM		4 CB	VAL C 176	20.42				
60			5 CG1	VAL C 176	21.38			_	_
	MOTA		6 CG2	VAL C 176	20.90	0 60.94	., -0.23		•

PCT/EP01/01457

			_	17	_	19.869	64.532	39.368	1.00 67.12	6
	MOTA	4687	C 7	/AL C 17	6		64.589	38.956	1.00 67.64	8
	MOTA	4688	0 7	VAL C 17	5	20.786	65.447	39.075	1.00 68.63	7
	MOTA	4689	N '	THR C 17	7	20.482	66.573	38.200	1.00 69.48	6
_	MOTA	4690	CA '	THR C 17	7	20.215	67.861	39.004	1.00 69.26	6
5	MOTA	4691	CB '	THR C 17	7	21.310	68.109	39.894	1.00 68.92	8
	MOTA	4692		THR C 17		18.932	67.718	39.804	1.00 68.40	6
	MOTA	4693		THR C 17		21.640	66,813	37.245	1.00 70.44	6
	MOTA	4694	С	THR C 17		22.802	66.641	37.614	1.00 69.76	8
	MOTA	4695	0	THR C 17	17	21.312	67.207	36.018	1.00 71.94	7
10	MOTA	4696		GLN C 17	78	22.320	67.470	34.998	1.00 73.43	6
	MOTA	4697		GLN C 1	/8	22.320	66.500	33.831	1.00 76.20	6
	MOTA	4698	СВ	GLN C 1		21.560	65.148	34.220	1.00 80.00	6
	MOTA	4699	CG	GLN C 1	/8	21.896	64.046	33.196	1.00 83.21	6
	MOTA	4700	· CD	GLN C 1	/8	21,745	64.237	31.973	1.00 84.40	8
15	MOTA	4701	OE1	GLN C 1	78 	21,745	62.889	33.694	1.00 82.90	7
	MOTA	4702	NE2	GLN C 1	78		68.884	34.482	1.00 72.16	6
	MOTA	4703	С	GLN C 1	78	22.149	69.244	34.044	1.00 72.49	8
	MOTA	4704	0	GLN C 1	78	21.070	69.675	34.522	1.00 71.74	7
	MOTA	4705	N	LYS C 1	79	23.214	71.054	34.048	1.00 71.38	6
20	MOTA	4706	CA	LYS C 1	79	23.166	72.022	35.233	1.00 73.17	6
	MOTA	4707	CB	LYS C 1	.79	23.205	71.610	36.380	1.00 78.41	6
	MOTA	4708	CG	LYS C 1	.79	22.291	72.459	37.644	1.00 79.07	6
	MOTA	4709	CD	LYS C 1	.79	22.499	72.433	38.864	1.00 80.35	6
	MOTA	4710	CE	LYS C 1	.79	21.814	70.452	39.163	1.00 81.10	7
25	MOTA	4711		LYS C 1	.79	22.363	70.432		1.00 70.13	6
	MOTA	4712	C	LYS C 1	L79	24.384	71.351	33.681	1.00 70.65	8
	MOTA	4713	0	LYS C	L79	25.504	71.466		1.00 68.21	7
	MOTA	4714	N	LYS C	180	24.180			CD OF	6
	MOTA	4715	CA.	LYS C	180	25.306	71.719 71.667			6
30	MOTA	4716	CB	rás c	180	24.833	72.846			6
- 00	MOTA	471	7 · CG	LYS C	180	24.008				6
	MOTA	471		LYS C	180	24.908				6
	MOTA	471	9 CE	LYS C	180	25.645				7
	MOTA	472		LYS C	180	24.768				6
35	MOTA	472	1 C	LYS C	180	25.971	73.075			8
	MOTA	472	2 0	LYS C	180	25.552				7
	MOTA		з и	ASN C	181	27.027				6
	ATOM		4 CA	ASN C	181	27.698	•	<u>-</u> .) 6
	ATOM		5 CB			27.967		_		2 6
40			6 CG	ASN C	181	28.580				7 8
,	ATOM		7 OF	1 ASN C	181	29.50	_	· _		7
	ATOM		8 NE	2 ASN C	181	28.07				96
	ATOM		29 C	ASN C	181	28.97				78
	ATOM		30 0	ASN C	181	29.93			1	3 7
45			31 N	SER C	182	28.97		·		8 6
	MOTA		32 CI	A SER C	182	30.13	•			26
	OTA		33 CI	3 SER C	182	29.72				9 8
	ATO		34 00	SER C	182	30.73				3 6
	ATO			SER C	182	31.23				2 8
50			36 O	SER C	182	30.94				6 7
	ATO		37 N	VAL C	183	32.48		·		5 6·
	ATO		38 C	A VAL C	183	33.61				
	ATO		39 C	B VAL C	: 183	33.87				
	OTA		40 C	G1 VAL C	183	33.64				75 6
5	5 ATO		41 C	G2 VAL C	183	35.29				38 6
J	. ATO		42 C	VAL (183	34.92				10 8
	ATO		43 C	VAL (183	35.3				99 7
	OTA		44 N	THR (184	35.63				
	ATC			A THR	C 184	36.8		_		
F	OTA O		746 (B THR	C 184	36.9				40 8
	OTA OC		747	G1 THR	C 184	35.9	81 80.3	20./	3, 1.00 00.	-
	•	<u>-</u>								

PCT/EP01/01457

					-130				-
	MOTA	4748	CG2 I	THR C 184	38.370	80.406		1.00 66.48	6
	MOTA	4749	C	THR C 184	38.032			1.00 70.57	6
		4750		THR C 184	37.920			1.00 70.99	8
	MOTA			TYR C 185	39.118	77.869		1.00 70.74	7
5	MOTA	4751		TYR C 185	40.236	77.572		1.00 71.98	6
5	MOTA	4752		ryr C 185	40.555	76.067		1.00 72.58	6
	MOTA	4753			39.351	75.195	29.937	1.00 72.59	6
	MOTA	4754		TYR C 185	38.363	75.011	28.970	1.00 73.55	6
	MOTA	4755		TYR C 185		74.258		1.00 72.54	6
	MOTA	4756		TYR C 185	37.224		31.185	1.00 72.27	6
10	MOTA	4757	CD2	TYR C 185	39.164	74.597	31.461	1.00 71.72	6
	MOTA	4758	CE2	TYR C 185	38.017	73.839		1.00 71.73	6
	ATOM	4759		TYR C 185	37.057	73.678	30.480	1.00 71.73	8
	ATOM	4760	OH	TYR C 185	35.920	72.951	30.732	1.00 71.30	6
	MOTA	4761		TYR C 185	41.426	78.355	29.191		8
15	ATOM	4762		TYR C 185	41.625	78.492	27.983	1.00 74.41	
13		4763		SER C 186	42.220	78.869	30.125	1.00 75.63	7
	MOTA			SER C 186	43.405	79.653	29.772	1.00 77.64	6
	MOTA	4764		SER C 186	44.183	80.015	31.043	1.00 77.47	6
	MOTA	4765	CB	SER C 186	44.398	78.870	31.858	1.00 78.93	8
	MOTA	4766	OG	SER C 100	44.300	78.875	28.793	1.00 77.75	6
20	MOTA	4767	С	SER C 186	44.926	79.457	27.893	1.00 76.44	8
	MOTA	4768	0	SER C 186		77.556	28.977	1.00 78.65	7
	MOTA	·4769	N	CYS C 187	44.332		28.135	1.00 79.38	6
	MOTA	4770	CA	CYS C 187	45,116	76.648	26.715	1.00 79.55	6
	MOTA	4771	С	CYS C 187	44.658	76.703		1.00 79.09	8
25	MOTA	4772	0	CYS C 187	45.443	76.687	25.771	1.00 79.04	6
	MOTA	4773	CB	CYS C 187	44.899	75.178	28.529	1.00 /3.04	16
	MOTA	4774	SG	CYS C 187	43.205	74.462	28.241	1.00 80.14	
		4775	N	CYS C 188	43.345	76.774	26.589	1.00 80.45	7
	MOTA		CA	CYS C 188	42.727	76.642	25.305	1.00 79.63	6
-00	MOTA	4776		CYS C 188	41.779	77.755	24.835	1.00 79.24	6
30	MOTA	4777	С	CYS C 188	40.785	78.065	25.504	1.00 81.46	8
	MOTA	4778	0		42.037	75.269	25.365	1.00 79.66	6
	MOTA	4779	CB	CYS C 188	42.984		26.264	1.00 75.61	16
	MOTA	4780	SG	CYS C 188	42.070	78.346	23.656	1.00 77.55	7
	MOTA	4781	N	PRO C 189		77.849	22.879	1.00 76.91	6
35	MOTA	4782	CD	PRO C 189	43.222		22.922	1.00 75.67	6
	MOTA	4783	CA	PRO C 189	41.378		21.502	1.00 75.82	6
	MOTA	4784	CB	PRO C 189	41.921		21.747	1.00 77.27	6
	ATOM	4785	CG	PRO C 189	43.328		22.927	1.00 73.97	6
	MOTA	4786	С	PRO C 189	39.835			1.00 73.90	8
40	MOTA	4787		PRO C 189	39.233	80.403	23.459	1.00 73.30	7
70	MOTA	4788		GLU C 190	39.201		22.317	1.00 /1.65	6
		4789		GLU C 190	37.734	78.404		1.00 68.61	
	MOTA	4790		GLU C 190	37.305	77.497			6
	MOTA			GLU C 190	38.277	77.434	19.945	1.00 72.05	6
4.5	MOTA			GLU C 190	38.082		18.969	1.00 73.59	6
45					36.908		18.657	1.00 73.46	8
	MOTA				39.10			1.00 77.52	8
	MOTA			2 GLU C 190	37.08			1.00 64.48	6
	MOTA			GLU C 190	37.76				8
	MOTA	479	6 0	GLU C 190					7
50	MOTA (479	7 N	ALA C 191	35.76				6
	ATOM	479	8 CA	ALA C 191	35.03	_			6
	ATOM		9 CB	ALA C 191	33.75				6
	MOTA			ALA C 191	34.70				8
	ATOM			ALA C 191	34.42		5 23.458		
55				TYR C 192	34.71	7 75.08			
36				100	34.40				
	MOTA			- 400	35.62	1 72.82			6
	ATO			~ 100	36.73		5 25.09		
	ATO)5 CC	o1 TYR C 192	37.69				_
_	OTA			E1 TYR C 192	38.68				
6				51 TIK C 192	36.80			9 1.00 56.77	76
	OTA	M 480) B CI	O2 TYR C 192	30.00				

PCT/EP01/01457

					-1J1	71 074	23.121	1.00 57.49	6
	MOTA	4809	CE2 TY	R C 192	37.785	71.874	23.119		6
	MOTA	4810	CZ TY	R C 192	38.720	72.898			8
	MOTA	4811	OH TY	R C 192	39.689	72.918			6
	MOTA	4812	C TY	R C 192	33.204	73.295 73.241		1.00 57.40	8
5	MOTA	4813		R C 192	33.292	73.241	25.836	1.00 57.28	7
	MOTA	4814		U C 193	32.084		26.506	1.00 58.77	6
	MOTA	4815		U C 193	30.839	72.678		1.00 59.02	6
	MOTA	4816	CB GL	υ C 193	29.681	72.597	-	1.00 61.64	6
	MOTA	4817	CG GL	U C 193	29.342	73.912	24.823 23.945	1.00 63.79	6
10	MOTA	4818		υ C 193	28.118	73.827		1.00 66.05	8
. •	MOTA	4819	OE1 GI	JU C 193	27.107	73.242	24.411	1.00 63.82	8
	MOTA	4820	OE2 GI	U C 193	28.171	74.355	22.805	1.00 58.56	6
	ATOM	4821	C GI	LU C 193	30.968	71.336	27.224	1.00 58.35	8
	ATOM	4822	O GI	ւՄ С 193	31.749	70.471	26.811	1.00 57.04	7
15	MOTA	4823	N AS	SP C 194	30.197	71.171	28.296	1.00 57.30	6
10	MOTA	4824	CA AS	SP C 194	30.215	69.940	29.059	1.00 57.30	6
	ATOM	4825	CB A	SP C 194	31.473	69.849	29.932	1.00 58.91	· 6
	MOTA	4826	CG A	SP C 194	31.430	70.777	31.141	1.00 57.40	8
	MOTA	4827	OD1 A	SP C 194	32.220	71.742	31.172	1.00 57.40	8
20	MOTA	4828	OD2 A	SP C 194	30.614	70.538	32.060	1.00 56.78	6
20	MOTA	4829	C A	SP C 194	28.982	69.848	29.933	1.00 56.76	8
		4830	0 A	SP C 194	28.411	70.864	30.320	1.00 56.90	7
	MOTA	4831	N V	AL C 195	28.567	68.619	30.223	1.00 55.47	6
	MOTA	4832	CA V	AL C 195	27.404	68.373	31.061	1.00 55.52	6
OE.	MOTA	4833	CB V	AL C 195	26.538	67.236	30.504	1.00 54.50	6
25	MOTA	4834	CG1 V	AL C 195	25.469	66.841	31.511	1.00 52.44	6
	MOTA	4835	CG2 V	AL C 195	25.914	67.671	29.199	1.00 55.96	6
	MOTA	4836	C Z	/AL C 195	27.874	67.973	32.444	1.00 56.12	8
	MOTA	4837	7 0	/AL C 195	28.661	67.046		1.00 56.74	7
20	MOTA	4838	N (SLU C 196	27.388	68.675		1.00 56.91	6
30	MOTA		CA	GLU C 196	27.777		34.816	1.00 57.46	6
	MOTA	4839 4840	CB (GLU C 196	28.051	69.654		1.00 58.09	6
	MOTA			GLU C 196	28.548	69.445	36.972	1.00 59.59	6
	MOTA	4841		GLU C 196	28.730	70.758		1.00 62.33	8
0-	MOTA	4842	_	GLU C 196	29.523	71.594	37.229	1.00 62.53	8
35		4843		GLU C 196	28.074		38.746	1.00 65.85	6
	MOTA	4844		GLU C 196	26.636	5 67.62°		1.00 57.05	8
	MOTA	4845	_	GLU C 196	25.517		35.487		7
	MOTA			VAL C 197	26.91	4 66.42	7 35.938		6
40	MOTA	4847		VAL C 197	25.88	9 65.61			
40		4848	-	VAL C 197	25.86	7 64.17	9 35.984		6 6
	MOTA		CC1	VAL C 197	24.77	7 63.36			6
	MOTA		_	VAL C 197	25.62	9 64.23	9 34.486		
	MOTA			VAL C 197	26.19	9 65.54	6 38.041		6
4-	MOTA		_	VAL C 197	27.32	0 65.20		1.00 58.31	8
45			-	SER C 198	25.21	4 65.88	5 38.866	1.00 57.35	7
	MOTA		T -:-	SER C 198	25.40	_	7 40.30	1.00 57.08	6
	ATOM			SER C 198	24.86		7 40.943		6
	MOTA			SER C 198	25.66	1 68.24			8
_	MOTA			SER C 198	24.71	.7 64.64	3 40.88		6
50				SER C 198	23.51		0 40.73		8
	MOTA			LEU C 199	25.49			1 1.00 57.83	7
	MOTA			LEU C 199	24.93		42.12		6
	IOTA			LEU C 199	25.82			4 1.00 56.00	6
	OTA			DEO C 199	25.4			6 1.00 56.43	6
5				LEU C 199	24.0			1 1.00 53.65	6
	OTA			LEU C 199	26.4			5 1.00 55.64	. 6
	OTA			LEU C 199	24.8	_		3 1.00 58.48	
	ATO:			LEU C 199	25.8	·		7 1.00 59.73	8
	OTA			LEU C 199	23.5			0 1.00 58.64	1 7
6	ota 08			ASN C 200 ASN C 200	23.3	_		- 4 00 50 4	1 6
	OTA	M 48	69 CA	ASN C 200	20.0	 :-			

PCT/EP01/01457

						-1,52				_
	MOTA	4870	СВ	ASN C 20	0	22.285			1.00 60.17	6
	ATOM	4871		ASN C 20		21.985	64.387		1.00 62.50	6
	ATOM	4872		ASN C 20		22.905	64.419	48.070	1.00 64.15	8
	MOTA	4873	ND2	ASN C 20		20.700	64.480	47.583	1.00 61.21	7
5	ATOM	4874		ASN C 20		22.898	61.801	45.988	1.00 55.97	6
0		4875	0	ASN C 20		21.821	61.316	45.627	1.00 54.75	8
	MOTA	4876	N	PHE C 20		23.739	61.181	46.802	1.00 53.51	7
	MOTA			PHE C 20		23.454	59.867	47.330	1.00 53.54	6
	MOTA	4877	CA			24.169	58.807	46.503	1.00 50.74	6
40	MOTA	4878	CB			25.663	58.820	46.677	1.00 48.36	6
10	MOTA	4879	CG	PHE C 20			57.763	47.309	1.00 45.72	6
	MOTA	4880		PHE C 20		26.312		46.252	1.00 46.85	6
	MOTA	4881	CD2	PHE C 20	1	26.413	59.912		1.00 43.95	6
	MOTA	4882	CE1	PHE C 20	1	27.689	57.794	47.521	1.00 45.93	6
	ATOM	4883	CE2	PHE C 20		27.782	59.955	46.457		6
15	ATOM	4884	CZ	PHE C 20		28.425	58.889	47.096	1.00 44.09	6
	MOTA	4885	С	PHE C 20	1	23.979	59.812	48.749	1.00 55.36	
	MOTA	4886	0	PHE C 20	1	24.640	60.739	49.210	1.00 53.66	8
	MOTA	4887	N	ARG C 20	2	23.698	58.702	49.425	1.00 57.35	7
	MOTA	4888	CA	ARG C 20		24.140	58.511	50.792	1.00 59.95	6
20	ATOM	4889	СВ	ARG C 20		23.192	59.224	51.744	1.00 62.36	6
20	ATOM	4890	CG	ARG C 20		21.844	58.529	51.789	1.00 64.26	6
			CD	ARG C 20		20.831	59.278	52.610	1.00 67.26	6
	MOTA	4891		ARG C 20		19.555	58.567	52.620	1.00 70.54	7
	ATOM	4892	NE	ARG C 20		18.430	59.062	53.129	1.00 69.46	6
0.5	MOTA	4893	CZ			18.420	60.270	53.670	1.00 69.25	7
25	MOTA	4894	NHT	ARG C 2	02	17.315	58.349	53.095	1.00 69.56	7
	MOTA	4895		ARG C 2	02	24.116	57.023	51.119	1.00 60.80	6
	MOTA	4896	С	ARG C 2			56.231	50.445	1.00 60.45	8
	MOTA	4897	0	ARG C 2		23.439		52.158	1.00 61.42	7
	MOTA	4898	N	LYS C 2		24.860	56.651	52.603	1.00 60.82	6
30	MOTA	4899	CA	LYS C 2		24.886	55.270	53.703	1.00 59.66	6
	MOTA	4900	CB		03	25.931	55.088		1.00 61.19	6
	MOTA	4901	CG	LYS C 2		25.988	53.688	54.258	1.00 63.27	6
	MOTA	4902	CD	LYS C 2	03	26.955	53.617	55.404		6
	MOTA	4903	CE	LYS C 2	03	27.036	52.209	55.947	1.00 66.98	7
35	MOTA	4904	NZ	LYS C 2	03	27.621	51.250	54.945	1.00 68.80	
-	ATOM	4905		LYS C 2		23.477	55.037	53.157	1.00 60.81	6
	MOTA	4906		LYS C 2		22.878	55.942	53.735	1.00 60.52	8
	MOTA	4907		LYS C 2	04	22.913	53.858	52.944	1.00 60.36	7
	ATOM	4908		LYS C 2	04	21.584	53.606	53.466	1.00 60.22	6
40	MOTA	4909		LYS C 2	04	21.017	52.329	52.837	1.00 58.64	6
40		4910		LYS C 2	04	20.591	52.487	51.381	1.00 55.82	6
	MOTA			LYS C 2		20.445	51.140	50.692	1.00 51.95	6
	MOTA	4911		LYS C 2		19.975		49.253	1.00 52.70	6
	MOTA	4912		LYS C 2	204	19.967		48.458	1.00 51.76	7
45	MOTA	4913		LYS C 2	004	21.742		54.977	1.00 62.01	6
45	MOTA	4914		LYS C 2	204	22.711		55.440	1.00 63.36	8
	MOTA	4915				20.811		55.747	1.00 62.55	7
	MOTA	4916		GLY C	205			57.202	1.00 62.30	6
	MOTA	4917		GLY C	205	20.898		57.844	1.00 61.75	6
	MOTA	4918	3 C	GLY C	205	19.797		57.093	1.00 60.18	8
50	MOTA	4919	OT	1 GLY C	205	18.911			1.00 60.86	8
	MOTA	4920	TO C	2 GLY C	205	19.811		59.092	1.00 71.47	6
	MOTA	492	1 CE	PHE D	1	39.182				
	ATOM	492	2 CG		1	40.239				6 6
	MOTA			1 PHE D	1	40.122	•			
55				2 PHE D	1	41.397				6
55	MOTA			1 PHE D	1	41.141				6
	MOTA			2 PHE D	1	42.418	3 71.835			6
					1	42.289	70.688			6
	MOTA MOTA			PHE D	1	37.07		2.658		6
60				PHE D	1	37.607		3.688		8
80				PHE D	1	37.01			1.00 69.08	7
	MOTA	433	0 14		-	<u>-</u> 				

PCT/EP01/01457

							-133				6
	MOTA	4931	CA I	PHE D	1		37.756	71.268		1.00 69.54	
	ATOM			ASP D	2		35.915	70.338		1.00 67.84	7
		4933		ASP D	2		35.253	70.061		1.00 66.03	6
	MOTA	4934		ASP D	2		33.949	69.266	3.772	1.00 66.47	6
_	MOTA		_	ASP D	2		34.138	68.032	2.928	1.00 68.89	6
5	MOTA	4935			2		35.029	67.218	3.287	1.00 68.16	8
	MOTA	4936		ASP D	2		33.396	67.886	1.912	1.00 70.47	8
	MOTA	4937		ASP D			36.181	69.310	4.933	1.00 64.63	6
	MOTA	4938	_	ASP D	2			69.165	4.672	1.00 64.43	8
	MOTA	4939		ASP D	2		37.378	68.837	6.049	1.00 62.26	7
10	MOTA	4940	N	ARG D	3		35.639		7.029	1.00 60.44	6
	MOTA	4941	CA	ARG D	3		36.461	68.128		1.00 60.90	6
	MOTA	4942	CB	ARG D	3		35.748	68.078	8.388	1.00 60.90	6
	MOTA	4943		ARG D	3		36.068	69.254	9.302	1.00 60.80	6
	ATOM	4944		ARG D	3		35.185	69.243	10.532	1.00 65.18	
4 5		4945	NE	ARG D	3		35.849	69.838	11.696	1.00 66.90	7
15	MOTA			ARG D	3		36.028	71.141	11.888	1.00 66.63	6
	MOTA	4946	CZ		3		35.591	72.031	11.002	1.00 68.16	7
	MOTA	4947		ARG D	3		36.664	71.553	12.964	1.00 66.33	7
	MOTA	4948		ARG D			36.831	66.719	6.580	1.00 59.10	6
	ATOM	4949	С	ARG D	3			66.252	6.845	1.00 57.28	8
20	MOTA	4950	0	ARG D	3		37.938		5.891	1.00 56.67	7
	ATOM	4951	N	ALA D	4		35.909	66.050		1.00 53.48	6
	MOTA	4952	CA	ALA D	4		36.153	64.699	5.414	1.00 52.26	6
	ATOM	4953	СВ	ALA D	4		34.938	64.175	4.706		6
	MOTA	4954	C	ALA D			37.347	64.696	4.479	1.00 53.39	8
05		4955	Ö	ALA D			38.225	63.851	4.600	1.00 52.40	
25	MOTA			ASP D	_		37.381	65.650	3.550	1.00 54.53	7
	MOTA	4956	N	ASP D			38.489	65.756	2.602	1.00 55.71	6
	MOTA	4957	CA				38.266	66.914	1.627	1.00 58.22	6
	MOTA	4958	CB	ASP D			36.938	66.810	0.881	1.00 61.46	6
	MOTA	4959	CG	ASP I			36.605	65.709	0.386	1.00 64.32	8
30	MOTA	4960		ASP I				67.832	0.773	1.00 63.22	8
	MOTA	4961	OD2	ASP I			36.227		3.326	1.00 54.28	6
	MOTA	4962	С	ASP I	5		39.816	65.970	2.914	1.00 52.86	8
	MOTA	4963	0	ASP I	5		40.844			1.00 52.53	7
	MOTA	4964	N	ILE I	5 6		39.787		4.410	1.00 53.69	6
35	MOTA	4965		ILE I			41.007		5.154	1.00 55.05	6
33		4966		ILE 1			40.813	68.128	6.191	1.00 55.79	
	MOTA						42.152	68.435	6.877	1.00 54.61	6
	MOTA	4967		LILE	_		40.266		5.499	1.00 55.83	6.
	MOTA	4968	CG.	T THE	D 6		40.121		6.400	1.00 55.01	6
	MOTA	4969		L ILE			41.545		5.870	1.00 52.43	6
40	MOTA	4970		ILE			42.711		5.709		8
	MOTA	4971	. 0	ILE							7
	MOTA	4972	2 N	LEU			40.701		7.401		6
	MOTA		CA		D 7		41.11				6
	MOTA		4 CB	LEU	D 7		39.96				6
45				LEU	D 7		39.601				6
70	MOTA			1 LEU	D 7		38.26	7 64.084			6
				2 LEU			40.68	7 64.356	10.440		
	MOTA			LEU.	_		41.52			1.00 51.80	6
	MOTA				_		42.50			l 1.00 52.35	8
	ATOM			LEU	_		40.78			5 1.00 52.55	7
50	MOTA (TYR			41.06	_		8 1.00 53.16	6
	ATOM	1 498	1 CA				_			4 4 -	6
	MOTA	1 498	2 CE				40.04		_	40	6
	MOTA		3 CG				40.29		_		6
	ATON		4 CI	ol TYR	D 8	3	40.03		_		6
5		_		1 TYR	D 8	3	40.30	8 58.772	2 1.06		
5:			וא פו	2 TYR	D 8		40.84				6
	1OTA			E2 TYR			41.13	60.61			6
	OTA				_	3	40.86		4 -0.11	2 1.00 61.47	7 6
	IOTA					3 B	41.16		3 -1.14		8
	ATO					в В	42.48	-		5 1.00 53.38	3 6
6			_		_		43.19	· ·			1 8
	ATO!	м 499	91 0	TYR	י ע	8	45.13	,, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			

PCT/EP01/01457

						-154				
	3 mOM	4992	N Z	ASN D	9	42.900	63.121	3.416	1.00 53.53	7
	MOTA MOTA	4993		ASN D	9	44.238	63.329	2.890	1.00 55.79	6
	MOTA	4994		ASN D	9	44.451	64.800	2.509	1.00 59.06	6
	MOTA	4995		ASN D	9	43.588	65.232	1.317	1.00 63.96	6
5	MOTA	4996		ASN D	9	42.912	64.406	0.688	1.00 67.47	8
J	ATOM	4997		ASN D	9	43.612	66.527	1.000	1.00 65.39	7
	ATOM	4998		ASN D	9	45.283	62.901	3.907	1.00 55.13	6 8
	ATOM	4999	0	ASN D	9	46.175	62.117	3.593	1.00 54.15	7
	MOTA	5000		ILE D	10	45.167	63.416	5.129	1.00 55.13 1.00 54.61	6
10	MOTA	5001	CA	ILE D	10	46.099	63.077	6.195	1.00 54.44	6
	MOTA	5002	CB	ILE D	10	45.660	63.693	7.53 4 8.651	1.00 53.71	6
	MOTA	5003		ILE D	10	46.585	63.218 65.222	7.435	1.00 52.93	6
	MOTA	5004		ILE D	10	45.683 45.083	65.222	8.605	1.00 47.92	6
	MOTA	5005			10	45.003	61.566	6.365	1.00 56.15	6
15	MOTA	5006	C	ILE D	10	47.258	60.992	6.496	1.00 57.11	8
	MOTA	5007	0	ILE D	10 11	45.018	60.927	6.363	1.00 56.48	7
	MOTA	5008	N	ARG D	11	44.938	59.494	6.512	1.00 58.41	6
	MOTA	5009	CA	ARG D	11	43.478	59.070	6.428	1.00 63.58	6
00	MOTA	5010 5011	CB CG	ARG D	11	43.229	57.585	6.631	1.00 70.33	6
20	MOTA	5011	CD	ARG D	11	43.398	57.219	8.100	1.00 79.03	6
	MOTA MOTA	5012	NE	ARG D	11	42.703	55.980	8.448	1.00 85.37	7
	ATOM	5014	CZ	ARG D	11	41.466	55.685	8.037	1.00 88.61	6
	MOTA	5015	NH1		11	40.795	56.548	7.249	1.00 89.11	7 7
25	MOTA	5016	NH2		11	40.890	54.545	8.434	1.00 87.93 1.00 58.93	6
	MOTA	5017	С	ARG D	11	45.721	58.778	5.425	1.00 58.85	8
	MOTA	5018	0	ARG D		46.497	57.862	5.698	1.00 50.05	7
	MOTA	5019	N	GLN D		45.507	59.211	4.186 3.024	1.00 57.95	6
	MOTA	5020	CA	GLM D		46.131	58.596 58.958	1.780	1.00 57.48	6
30	MOTA	5021	CB	GLN D	_	45.345		0.955	1.00 61.67	6
	MOTA	5022	CG	GLN D		44.961 43.773		1.525	1.00 61.71	6
	MOTA	5023	CD	GLN D		42.729		1.698	1.00 64.71	8
	MOTA	5024		GLN D		43.912		1.831	1.00 59.81	7
0.5	MOTA	5025	NE2	GLN C		47.589		2.769	1.00 57.99	6
35	MOTA	5026		GLN I		48.280		2.097	1.00 58.62	8
	MOTA	5027		THR I		48.070		3.291	1.00 57.97	7
	MOTA	5028 5029		THR I		49.452	60.433	3.042	1.00 58.22	6
	MOTA	5030		THR I		49.520		2.464		6
40	MOTA MOTA	5031		1 THR I		48.907		3.377		8 6
40	MOTA	5032				48.808		1.110		6
	MOTA	5033		THR I	D 13	50.363		4.255		8
	MOTA	5034		. THR	D 13	51.589		4.120 5.440		7
	MOTA	5035		SER !		49.76		6.669		6
45	MOTA	503	6 CA			50.54		7.863		6
	MOTA	5037				49.63		8.988		8
	MOTA					50.41° 51.32		6.903		6
	MOTA			SER		50.92		6.467	1.00 62.07	8
	MOTA			SER		52.44		7.596	1.00 59.21	7
50				ARG ARG		53.31		7.913	1.00 58.97	6
	MOTA			_		54.55		7.013	1.00 59.72	6
	ATOM					54.21			3 1.00 62.38	6
	ATOM			_		55.45		4.73	8 1.00 63.96	6
==	MOTA					56.01				7
55	MOTA (_		57.20	7 55.873			6
	MOTA		8 N	H1 ARG		57.98	56.528			7 7
	MOTA			H2 ARG		57.62				
	MOTA			ARG		53.72				
60						54.70				
	OTA		52 N	PRO	D 16	52.96	57 57.517	10.20		

PCT/EP01/01457

						-122			1 00 E1 06	6
	MOTA	5053	CD	PRO D	16	51.785	56.700		4.00	6
	MOTA	5054	CA	PRO D	16	53.200	57.524		1.00 O= ·	
		5055	СВ	PRO D	16	52.104	56.602		1.00 15.00	6
	MOTA	5056	CG	PRO D	16	51.031	56.720	11.226	1.00 51.02	6
-	MOTA		C	PRO D	16	54.580	57.066	12.130	1.00 49.97	6
5	MOTA	5057			16	55.034	57.387	13.220	1.00 48.83	8
	MOTA	5058	0	PRO D		55.247	56.313	11.270	1.00 50.05	7
	MOTA	5059	N	ASP D	17	56.568	55.809	11.612	1.00 53.82	6
	MOTA	5060	CA	ASP D	17	56.796	54.419	10.981	1.00 57.43	6
	MOTA	5061	CB	ASP D	17		53.320	11.666	1.00 63.55	6
10	ATOM	5062	CG	ASP D	17	55.979		12.892	1.00 63.43	8
	MOTA	5063		ASP D	17	55.728	53.431		1.00 66.47	8
	MOTA	5064	OD2	ASP D	17	55.598	52.330	10.985	1.00 52.72	6
	ATOM	5065	С	ASP D	17	57.710	56.733	11.218	1.00 54.00	8
	ATOM	5066	0 -	ASP D	17	58.875	56.406	11.440		7
15	MOTA	5067	N	VAL D		57.384	57.888	10.653	1.00 50.54	6
13		5068	CA	VAL D		58.418	58.808	10.209	1.00 51.72	
	MOTA		CB	VAL I		58.353	58.992	8.680	1.00 52.70	6
	MOTA	5069		L VAL E		59.487	59.869	8.209	1.00 52.67	6
	MOTA	5070				58.426	57.642	7.998	1.00 53.16	6
	MOTA	5071		2 VAL I		58.402	60.181	10.865	1.00 51.90	6
20	MOTA	5072	С	VAL I		57.463	60.955	10.716	1.00 50.79	8
	MOTA	5073	0	VAL I			60.473	11.586	1.00 52.81	7
	MOTA	5074	N	ILE I		59.475	61.748	12.280	1.00 54.09	6
	MOTA	5075	CA	ILE I	19	59.646		13.116	1.00 53.08	6
	MOTA	5076	CB	ILE I		60.960	61.699		1.00 53.31	6
25	ATOM	5077	CG	2 ILE	D 19	62.168		12.194	1.00 52.13	6
20	MOTA	5078		1 ILE	D 19	61.074	62.919	14.027	1.00 32.13	6
		5079		1 ILE		62.157	62.753	15.086		6
	MOTA			ILE		59.675	62.907	11.255	1.00 56.58	8
	MOTA	5080		ILE		60.436	62.877	10.274	1.00 57.79	
	MOTA	5081		PRO	-	58.833		11.464	1.00 56.89	7
30	MOTA	5082		_		57.915		12.603	1.00 56.43	6
	MOTA	5083		_		58.725		10.587	1.00 58.17	6
	MOTA	5084	4 C <i>P</i>			57.505		11.148	1.00 57.33	6
	MOTA	508	5 CE				·		1.00 56.81	6
	MOTA	5080	6 CC			56.812			1.00 60.38	6
35	MOTA	508	7 C	PRO		59.985			1.00 57.93	8
	MOTA	508	8 0	PRO	D 20	59.920			1.00 64.41	7
	MOTA	508	9 N	THR	D 21	61.12			60 00	6
	ATOM	509		A THR	D 21	62.39				6
	ATOM	_	_			63.54	6 65.121			8
40			_	G1 THR		63.89				6
40				G2 THR		64.76				6
	MOTA		_	_		62.67				
	MOTA		_		_	62.48	0 66.45	7.936	1.00 75.27	8
	MOTA					63.13		7 9.285	1.00 77.41	7
	MOTA					63.48	_	6 8.203	1.00 81.17	6
45						62.79		6 8.428	1.00 82.19	6
	MOTA	509		B GLN	_	61.28			1.00 84.72	6
	MOTA	509		G GLN		60.68	71.41		9 1.00 86.15	6
	ATOM	i 510		D GLN						8
	ATOM			DE1 GLN		60.93				7
50			02 1	NE2 GLA	1 D 22	59.90		-		6
•	ATO			C GLI		65.00				. 8
	OTA			GL1		65.53				7
		•	-	N ARC	_	65.69				· .
	OTA				3 D 23	67.1	59 68.76		0 1.00 87.34	. 6
	OTA				GD 23	67.6		31 7.10	5 1.00 88.19	6
5			-			67.4			2 1.00 89.83	6
	OTA					66.2			4 1.00 92.72	
	ATO:		-			65.9			8 1.00 95.59	7
	ATO	м 51			G D 23			-		5 6
	OTA		.11		G D 23	66.9				
6	OTA O		12	NH1 AR	G D 23	68.1				
_	ATC		13	NH2 AR	.G D 23	66.5	55 73.2	20 2.25	,,	*

PCT/EP01/01457

WO 01/58951

MOTA

| See | Sec | See MOTA MOTA MOTA MOTA 5 ATOM MOTA MOTA MOTA MOTA 10 MOTA MOTA MOTA MOTA MOTA 15 MOTA ATOM MOTA MOTA MOTA 20 MOTA MOTA MOTA MOTA MOTA 25 MOTA MOTA MOTA MOTA MOTA MOTA 30 MOTA MOTA MOTA MOTA 35 MOTA MOTA MOTA MOTA MOTA 40 MOTA MOTA MOTA MOTA MOTA 45 ATOM MOTA MOTA MOTA MOTA 50 ATOM MOTA MOTA MOTA MOTA 55 MOTA MOTA MOTA MOTA MOTA 60 MOTA

- ----

PCT/EP01/01457

							-137				_
	х пом	5175	CA	SER I	n .	32	54.062	70.594		1.00 59.47	6
	MOTA					32	53.467	71.934	29.175	1.00 60.04	6
	MOTA	5176	CB	SER			52.892	. —		1.00 62.30	8
	MOTA	5177	OG	SER		32	53.023	69.799	30.433	1.00 58.78	6
_	MOTA	5178	С	SER		32			29.966	1.00 59.54	8
5	MOTA	5179	0	SER		32	51.906	69.572		1.00 56.81	. 7
	MOTA	5180	N	LEU		33	53.390	69.379	31.638		6
	MOTA	5181	CA	LEU	D	33	52.468	68.629	32.472	1.00 56.85	6
	MOTA	5182	СВ	LEU	D	33	53.217	67.702	33.426	1.00 54.23	
	ATOM	5183	CG	LEU		33	54.192	66.726	32.775	1.00 55.08	6
10	ATOM	5184		LEU		33	54.665	65.709	33.818	1.00 53.15	6
10				LEU		33	53.513	66.034	31.614	1.00 54.80	6
	MOTA	5185				33	51.623	69.572	33.291	1.00 56.91	6
	MOTA	5186	C	LEU			52.136	70.542	33.829	1.00 59.29	8
	MOTA	5187	0	LEU		33		69.294	33.366	1.00 56.10	7
	MOTA	5188	N	LYS		34	50.327		34.171	1.00 55.13	6
15	MOTA	5189	CA	LYS	D	34	49.422	70.089		1.00 58.38	6
	ATOM	5190	CB	LYS	D	34	48.311	70.694	33.320	1.00 56.50	6
	ATOM	5191	CG	LYS	D	34	48.802	71.519	32.146	1.00 65.52	
	ATOM	5192	CD	LYS	D	34	49.581	72.764	32.58 1	1.00.69.06	6
		5193	CE	LYS		34	50.100	73.559	31.364	1.00 72.37	6
20	MOTA		NZ	LYS		34	50.855	74.801	31.747	1.00 72.05	7
20	MOTA	5194				34	48.838	69.065	35.118	1.00 53.80	6
	MOTA	5195	C	LYS			48.123	68.167	34.685	1.00 55.04	8
	MOTA	5196	0	LYS		34	49.144	69.173	36.405	1.00 51.60	7
	MOTA	5197	N	PHE		35		68.200	37.346	1.00 49.19	6
	MOTA	5198	CA	PHE	D	35	48.616		38.616	1.00 46.49	6
25	ATOM	5199	CB	PHE	D	35	49.441	68.199		1.00 48.31	6
	MOTA	5200	CG	PHE	D	35	50.838	67.733	38.393	1.00 46.94	6
	ATOM	5201	CD1	PHE	D	35	51.823	68.617	37.964		6
	ATOM	5202		PHE		35	51.159	66.387	38.530	1.00 49.16	
	ATOM	5203		PHE		35	53.109	68.170	37.668	1.00 48.04	6
20		5204	CE2			35	52.449	65.925	38.235	1.00 50.28	6
30	ATOM			PHE		35	53.424	66.818	37.802	1.00 48.13	6
	MOTA	5205	CZ			35	47.136	68.352	37.642	1.00 49.07	6
	ATOM	5206	С	PHE			46.626	69.449	37.869	1.00 49.57	8
	MOTA	5207		PHE		35	46.451	67.217	37.600	1.00 47.68	7
	MOTA	5208	N	ILE		36		67.156	37.827	1.00 44.72	6
35	ATOM	5209	CA	ILE	; D	36	45.030		36.731	1.00 43.48	6
	ATOM	5210	CB	ILI	D	36	44.352	66.334		1.00 41.45	6
	ATOM	5211	. CG	2 ILE	D	36	42.850		36.914	1.00 43.86	6
	ATOM	5212		1 ILI	E D	36	44.752	66.877	35.360	1.00 45.00	6
	ATOM	5213		1 ILI	E D	36	44.398	68.324	35.152	1.00 46.64	
40	MOTA	5214			E D	36	44.719	66.525	39.164	1.00 44.81	6
40					3 D	36	43.677	66.798	39.743	1.00 46.51	8
	MOTA	5215			N D	37	45.612	65.678	39.661	1.00 42.08	7
	MOTA	5216				37	45.363		40.939	1.00 42.31	6
	MOTA	5217			1 D	37	44.117				6
	MOTA	5218			1 D						6
45	ATOM	5219			N D	37	43.392				8
	MOTA	5220	O OI	1 AS	N D	37	44.015				7
	ATOM	522	1 NE	2 AS	N D		42.068				6
	ATOM		2 C	AS	N D	37	46.539				8
	MOTA			AS	N D	37	47.380				
50					E D		46.58	3 63.977	42.740	1.00 43.93	
50					E D		47.613		43.372	1.00 44.58	6
	MOTA				E D		48.49		44.246	1.00 42.93	6
	ATOM						49.47			1.00 39.88	6
	MOTA		7 C	32 II	1E L	38					6
	MOTA			31 II	E	38	49.22		_		
55	MOTA	522	9 C	01 II			49.94				
	ATOM	523	0 C		EΙ		46.79				8
	ATOM			II	ΕI		46.16	9 62.565			
	ATOM			L	EU I	39	46.80		5 43.77		
	ATOM				EU I		45.97				. 0
60					EU I		45.48				
00	ATOL ATOL				ΣU I		44.83	4 59.72	3 42.14	1 1.00 54.64	1 6
	ATO		,								

PCT/EP01/01457

										•	
							-158	co 777	41.068	1.00 53.53	6
	MOTA	5236		LEU D	39		44.356		42.696	1.00 53.70	6
	MOTA	5237		LEU D	39		43.666 46.520		45.529	1.00 53.82	6
	MOTA	5238	_	LEU D	39 39		45.793	•••	46.479	1.00 54.77	8
_	MOTA	5239	0	LEU D	40		47.771	58.620	45.437	1.00 54.21	7
5	MOTA	5240	N CA	GLU D	40		48.349	57.825		1.00 56.24	6
	MOTA	5241 5242	CB	GLU D			48.278	56.339		1.00 58.19	6
	ATOM ATOM	5242	CG	GLU D	_		46.873	55.801		1.00 65.00	6
	ATOM	5244	CD	GLU D			46.844	54.291	45.938	1.00 68.23	6 - 8
10	ATOM	5245		GLU D			47.443	53.791	44.955	1.00 70.63	8
	ATOM	5246		GLU D			46.226	53.611	46.789	1.00 68.96 1.00 56.38	6
	ATOM	5247	С	GLU D	40		49.785	58.198	46.702 45.746	1.00 59.25	8
	ATOM	5248	0	GLU I			50.541	58.355	47.955	1.00 55.49	7
	MOTA	5249	N	VAL I			50.162	58.343	48.273	1.00 54.71	6
15	MOTA	5250	CA	VAL I			51.517 51.590	58.695 60.145	48.811	1.00 55.08	6
	MOTA	5251	CB	VAL			52.954	60.431	49.361	1.00 55.65	6
	MOTA	5252	CG1	VAL I) 41		51.273	61.125	47.696	1.00 55.07	6
	ATOM	5253		VAL I			52.003	57.713	49.309	1.00 54.17	6
	ATOM	5254	C	VAL I			51.232	57.239	50.136	1.00 53.51	8
20	MOTA	5255	0	ASN I			53.280	57,381	49.233	1.00 54.90	7
	MOTA	5256	N CA	ASN I			53.880	56.473	50.182	1.00 56.47	6
	MOTA	5257 5258	CB	ASN			53.944	55.056	49.612	1.00 55.97	6
	ATOM	5259	CG	ASN	_		54.306	54.025	50.661	1.00 56.38	6
25	ATOM ATOM	5260		ASN			55.272	54.191	51.408	1.00 55.15	8 7
25	ATOM	5261		ASN		:	53.536	52.947	50.717	1.00 56.12 1.00 58.56	6
	ATOM	5262	C	ASN		;	55.278	57.022	50.420 49.567	1.00 58.83	8
	ATOM	5263	0	ASN		}	56.154	56.912	51.579	1.00 59.69	7
	ATOM	5264	N	GLU			55.474	57.639	51.905	1.00 60.97	6
30	MOTA	5265	CA	GLU			56.771	58.208 59.192	53.065	1.00 63.50	6
	MOTA	5266	CB	GLU			56.640 57.921		53.341	1.00 67.19	6
	MOTA	5267		GLU			57.725		54.303	1.00 68.84	6
	MOTA	5268		GLU			58.743		54.682	1.00 70.83	8
	MOTA	5269		1 GLU	D 4		56.568		54.670	1.00 67.80	8
35	MOTA	5270		2 GLU			57.792		52.246	1.00 59.80	6
	MOTA	5271		GLU GLU			58.993		52.138	1.00 59.85	8
	MOTA	5272		ILE	_	4	57.301		52.653	1.00 59.27	7
	MOTA	5273 5274			_	4	58.164	§ 54.858			6 6
40	MOTA MOTA	527		·	_	4	57.373				6
40	ATOM	_				4	58.300				6
	ATOM		7 C	1 ILE		4	56.75				6
	ATOM			1 ILE	D 4	4	57.76				6
	ATOM			ILE	-	4	58.80				8
45	MOTA	528	0 0		-	14	60.00				7
	MOTA	528	1 N	THE		15	57.98			1.00 54.05	6
	ATOM	528				15	58.46 57.41			7 1.00 52.43	6
	ATOM				-	45	56.20			3 1.00 49.39	8
	MOTA			G1 THE		45 45	57.12			3 1.00 49.70	6
50				G2 THE		45	58.83		1 48.417		6
	ATOM					45	59.42		5 47.39		8
	MOTA					46	58.49		9 48.66		7
	ATOM					46	58.79	6 56.87			6
55	ATON AOTO				N D	46	60.30				6
50	IOTA IOTA		-		N D	46	60.87				i 8
	OTA			D1 AS		46	62.05				
	ATO			ID2 AS		46	60.04			- 4 00 50 05	
	ATO			: AS	ИД	46	58.15		8 46.36 8 45.32		
6					N D	46	58.83				7
-	ATO:		96 1	4 GL	U D	47	56.8	20 20.24	40.57		

PCT/EP01/01457 WO 01/58951

```
MOTA
        MOTA
        MOTA
        MOTA
        MOTA
        MOTA
         MOTA
         MOTA
         MOTA
10
       MOTA
         MOTA
         MOTA
         MOTA
         MOTA
15
         MOTA
         MOTA
          MOTA
          MOTA
          MOTA
 20
          MOTA
          MOTA
          MOTA
          MOTA
           MOTA
 25
           MOTA
           MOTA
           MOTA
           MOTA
                                                                                                                                          8
           MOTA
  30
                                                                                                                                          7
           MOTA
                                                                                                                                        6
           MOTA
           MOTA
           MOTA
            MOTA
  35
           MOTA
            MOTA
            MOTA
                                                                                                                                           6
            MOTA
                                                                                                                                           6
            MOTA
   40
                                                                                                                                            6
            MOTA
             MOTA
                                                                                                                                            6
             MOTA
             MOTA
                                                                                                                                            6
             MOTA
   45 ATOM
                                                                                                                                            6
             MOTA
                                                                                                                                             6

      47.870
      64.940
      33.241
      1.00
      44.00

      47.606
      63.931
      32.610
      1.00
      46.55

      47.934
      66.133
      32.673
      1.00
      43.89

      47.726
      66.294
      31.253
      1.00
      44.08

      46.919
      67.538
      30.948
      1.00
      45.09

      45.537
      67.474
      31.396
      1.00
      46.86

      44.596
      68.542
      31.383
      1.00
      49.97

      43.372
      68.024
      31.855
      1.00
      50.77

      44.666
      69.891
      31.017
      1.00
      52.22

                                                                                                                                             8
             MOTA
             MOTA
                          5345 N
             MOTA
                                    CA TRP D
                                                         53
    50
                          5346
                                                                                                                                             6
              MOTA
                                    CB TRP D 53
              MOTA
                          5347
                                                                                                                                             6
                                     CG TRP D 53
                          5348
              MOTA
                                     CD2 TRP D 53
                           5349
              MOTA
                                     CE2 TRP D 53
                                                                      44.666 69.891 31.017 1.00 52.22
44.877 66.383 31.863 1.00 47.58
                           5350
              MOTA
                                      CE3 TRP D 53
                           5351
     55
              ATOM
                                      CD1 TRP D 53
                                                                                       66.700 32.141 1.00 48.69
              MOTA
                           5352
                                                                                                                    1.00 52.23
                                                                        43.571
                                      NE1 TRP D 53
                           5353
                                                                        42.222 68.808 31.973
              MOTA
                                      CZ2 TRP D 53
CZ3 TRP D 53
                                      CZZ TRP D 53 42.222 66.606 31.75 1.00 54.33 CZ3 TRP D 53 43.521 70.672 31.135 1.00 54.33 CH2 TRP D 53 42.313 70.126 31.610 1.00 53.10 C TRP D 53 49.085 66.452 30.640 1.00 46.17
                           5354
              MOTA
               MOTA
                           5355
     60
                           5356
               MOTA
                            5357
                                      С
               MOTA
```

PCT/EP01/01457

							-160					_
	» mom	5358	0	TRP D	53	,	49.803	67.384		1.00 46		8
	ATOM ATOM	5359	N	GLN I			49.444	65.532	29.760	1.00 49		7
	ATOM	5360	CA	GLN I			50.741	65.592	29.112	1.00 48		6
	ATOM	5361	СВ	GLN I		1	51.248	64.184	28.809	1.00 48		6
5	ATOM	5362	CG	GLN I	_		52.677	64.135	28.317	1.00 50		6
3	MOTA	5363	CD	GLN I			53.339	62.792	28.583	1.00 52		6
	MOTA	5364	OE1				53.409	62.336	29.721	1.00 52	.24	8
	ATOM	5365	NE2	GLN I			53.832	62.158	27.532	1.00 53		7
	ATOM	5366	C	GLN I			50.560	66.408	27.849	1.00 49	.01	6
10	ATOM	5367	Ö	GLN :	_		50.504	65.892	26.735	1.00 48		8 7
10	ATOM	5368	N	GLN		5	50.441	67.708	28.058	1.00 51		6
	ATOM	5369	CA	GLN	_	5	50.256	68.665	26.985	1.00 53	. 20	6
	MOTA	5370	CB	GLN		5	49.964	70.022	27.609	1.00 56		6
	ATOM	5371	CG	GLN		5	49.913	71.176	26.652	1.00 66		
15	MOTA	5372	CD	GLN		5	49.355	72.406	27.326	1.00 70)./2	6 8
13	MOTA	5372		GLN		5	49.611	72.637	28.525	1.00 7		7
	MOTA	5374		GLN		5	48.584	73.210	26.573	1.00 7	0.76	6
		5375	C	GLN		55	51.494	68.697	26.092	1.00 5		8
	MOTA	5376	Ö	GLN		5	52.533	69.249	26.457	1.00 5		.7
20	MOTA	5377	N	THR		56	51.373	68.091	24.920	1.00 4		
20	MOTA	5378	CA	THR		56	52.485	68.005	23.988	1.00 4	8.81	6 6
	MOTA MOTA	5379	CB	THR		56	52 <i>.</i> 769	66.534	23.617	1.00 4		8
	ATOM	5380		LTHR		56	52.793	65.733	24.801	1.00 5	0.12	6
	ATOM	5381	CG			56	54.101	66.408	22.925	1.00 4	7.54	6
25		5382		THR		56	52.198	68.771	22.709	1.00 4		8
20	MOTA	5383	ō	THR		56	51.051	68.862	22.275	1.00 5		7
	MOTA MOTA	5384		THR		57	53.243	69.320	22.101	1.00 4		6
	ATOM	5385				57	53.080	70.069	20.860	1.00 4		6
	ATOM	5386				57	52.766	71.563	21.126	1.00 4	10 11	8
30	MOTA	5387		1 THR		57	51.521		21.834	1.00 4	17 20	6
30	ATOM	5388				57	52.642		19.826			6
	ATOM	5389		THR		57	54.322		19.995			8
	ATOM	5390		THR		57	55.446		20.496			7
	ATOM	5393		TRE		58	54.113	69.928			46.03	6
35	ATOM	5392				58	55.221				45.JZ 46 N7	6
55	ATOM	539				58	55.890				46 21	6
	ATOM	539				58	55.05				40.2± 45 21	6
	MOTA	_	_	2 TRI		58	54.099				45.21 45 14	6
	ATOM		-	E2 TRI	P D	58	53.51	7 65.702		_	44 92	6
40	ATOM		-	E3 TRI	P D	58	53.67				44.73	6
40	ATOM		•	01 TR		58	55.01				46.01	7
	ATOM		9 N	E1 TR	PD	58	54.09				46.24	6
	ATOM			Z2 TR		58	52.53				45.62	6
	ATOM		1 C	Z3 TR	РD	58	52.69				45.70	6
45		40		H2 TR	рD	58	52.13				47.55	6
-,0	ATOM				PР	58	54.67				46.55	8
	ATOM			TR	PD	58	53.49	4 70.50	_		51.25	7
	ATOM			SE	R D	59	55.53				54.98	6
	ATOM				R D	59	55.09				56.59	6
50		_		B SE	RD	59	55.68				61.93	8
00	ATO				R D	59	54.96				55.53	6
	ATO				ER D	59	55.45				54.93	
	OTA				ER D	59	-56.58				57.49	7
	ATO				SP D	60	54.47				59.17	
55		-			SP D	60	54.6				61.53	6
٥.	ATO			B AS	SP D	60	53.8		6 11.31		63.57	6
	ATO:				SP D	60	54.1				64.52	
	OTA		15 (OD1 A	SP D	60	54.4				64.89	8
•	ATO		16	OD2 A	SP D	60	53.9				60.52	
6				C A	SP D	60	54.0				59.95	
	ATO				SP D	60	52.8	47 69.03	10 3.0.	1.00		
									•			

									-161						_
		-014	E 410	N	ARG	n	61		54.937	69.6	09	8.995	1.00 6	2.50	7
		TOM	5419		ARG		61		54.503	70.3	34	7.800	1.00 6	4.61	6
		TOM	5420	CA			61		55.672	71.1	137	7.205	1.00 6	57.57	6
		MOT	5421	CB	ARG				56.000	72.4		7.909	1.00	73.40	6
		TOM	5422	CG	ARG		61		56.968	73.2		7.037	1.00 8		6
5	A'	TOM	5423	CD	ARG		61		57.268	74.6		7.537	1.00	86.56	·7
	A	MOT	5424	NE	ARG		61			75.5		6.910	1.00		6
	A	TOM	5425	CZ	ARG		61		58.057			5.749	1.00	87 01	7
		MOT.	5426	NH1	ARG	D	61		58.642	75.2			1.00	87 16	7
		TOM	5427	NH2	ARG	D	61		58.246	76.		7.433	1.00		6
10		MOTA	5428	С	ARG	; D	61		53.867	69.		6.703	1.00		8
		MOTA	5429	ō	ARG	; D	61		53.145	69.		5.844	1.00	63.31	7
		MOTA	5430	N	THE		62		54.121	68.		6.722	1.00	62.13	6
			5431	CA	THE		62		53.542	67.	303	5.704	1.00		
		MOTA		CB	THE		62		54.171	65.	886	5.716	1.00	62.74	6
		MOTA	5432		THE		62		53.809	65.	201	6.924	1.00	65.20	8
15		MOTA	5433				62		55.692	65.	974	5.624	1.00	63.05	6
	1	MOTA	5434	CG2			62		52.030	67.	184	5.911	1.00	60.41	6
	2	MOTA	5435	С		R D			51.313		619	5.073	1.00	60.16	8
	1	MOTA	5436	0		R D	62		51.551		731	7.025	1.00	59.01	7
	1	MOTA	5437	N		U D	63				705	7.356	1.00	57.25	6
20	0 3	МОТА	5438	CA		Uρ	63		50.124			8.860		55.13	6
		MOTA	5439	CB	$r_{\rm E}$	UD	63		49.932		483	9.489		54.37	6
		MOTA	5440	CG	LE	υD	63		50.567		.242		1 00	51.58	6
		ATOM	5441	CD:	l LE	UD	63		50 <i>.</i> 396		. 277	10.997	1.00	55.32	6
		ATOM	5442		2 LE		63		49.917		.002	8.903	1.00	56.83	6
2	_		5443			U D	63		49.446		.017	6.973	1.00	50.03	8
~		MOTA	5444			U D	63		48.228	69	.091	6.904	1.00	55.62	7
		MOTA	5445			A D	64		50.241	70	.052	6.730		56.52	6
		MOTA				A D	64		49.702	71	.362	6.388		56.94	
		MOTA	5446			A D	64		50.843	72	.351	6.196	1.00	56.75	6
_		MOTA	5447				64		48.825		.336	5.147	1.00	57.08	6
3	30	MOTA	5448			LA D			49.091		.571	4.222	1.00	59.16	8
		MOTA	5449			D AL	64		47.785		.174	5.138	1.00	56.39	7
		MOTA	5450			RP D			46.853		.286	4.008	1.00	57.81	6
		MOTA	545	1 CA		RP D					.279	4.183	1.00	52.06	6
		ATOM	545	2 CE		RP D			45.718		.708	5.139		49.69	6
(35	MOTA	545	3 CC		RP D			44.662	_	.383	6.532		48.62	6
		ATOM	545	4 CI)2 T	RP D	65		44.574			7.027		50.58	6
		ATOM	545	5 CI	E2 T	RP D	65		43.386		.974	7.409		45.78	6
		MOTA		6 C		RP E			45.379		0.649	4.855		51.37	6
		ATOM			D1 T	RP I	65		43.563		2.466			51.62	7
	40	ATOM		8 N	E1 T	RP I	65		42.78	-	2.631	5.985	_	0 48.81	6
	40				Z2 I	RP I	· 65	,	42.98	•	1.849	8.35		0 45.33	6
		ATOM		0 0	Z3 T	ו פפי			44.98		0.525	8.73		0 45.33	6
		ATOM			н2 Т	RP I	0 65		43.79	7 7:	1.122	9.19	3 1.0	0 48.88	
		ATOM				RP I			46.28		3.723	3.87	_	0 60.73	6
		ATOM	546			RP I			46.30	9 7	4.493	4.83		0 61.78	8
	45	MOTA			_				45.75	7 7	4.081	2.69	2 1.0	0 63.62	7
		MOTA				ASN			45.19		5.423	2.47	4 1.0	0 66.29	6
		MOTA	1 546	65 C		ASN	_		44.99	_	5.702	0.97	5 1.0	0 67.13	6
		MOTA	1 546	66 C		ASN	-				7.129	0.70	0 1.0	0 70.42	6
		ATO1	1 54			ASN			44,46		7.560		_	0 68.84	. 8
	50	ATO		68 C	D1 .	ASN	D 6	6	44.31	. /	7,500			0 71.49	7
	ŲŪ.	ATO			1D2			6	44.16		7.866			0 67.74	
		ATO				ASN		6	43.88		5.676			0 67.73	7 8
						ASN		6	42.82		5.208			10 70 4	7
		ATO		• —		SER			43.98		76.466			00 70.41	
		ATO				SER		7	42.89		76.810			00 72.53	V 6
	55	ATO:				SER	_	7	43.3	63 7	77.028		36 1.0	00 71.50	0 6
		ATO			CB			7	42.5		77.911	7.32	24 1.	00 70.6	0 8
		ATO			OG	SER	_		42.0		78.025	5 4.70		00 74.9	0 6
		ATO			C	SER	_	57	41.1		78.434		30 1.	00 75.9	
		ATO	M 54		0	SER		57	42.2		78.60		89 1.	00 77.5	7 7
	60	ATC	M 54	-	N	SER		8			79.80			00 79.0	8 6
	_	ATC		179	CA	SER	D 6	58	41.5	30	, , , , , , , ,	_	- '		

```
-162
                                                                                                                                              41.991 80.243 1.761 1.00 78.86
41.612 79.297 0.776 1.00 79.93
40.012 79.707 3.157 1.00 80.32
                                                 5480 CB SER D 68
5481 OG SER D 68
5482 C SER D 68
                   MOTA
                                                                                                                                                                                                                                                                       1.00 79.93
                                             5481 OG SER D 68
5482 C SER D 68
5483 O SER D 68
5484 N HIS D 69
5485 CA HIS D 69
5485 CA HIS D 69
5485 CA HIS D 69
5486 CB HIS D 69
5487 CG HIS D 69
5487 CG HIS D 69
5487 CG HIS D 69
5488 CD2 HIS D 69
5488 CD2 HIS D 69
5489 ND1 HIS D 69
5489 ND1 HIS D 69
5490 CE1 HIS D 69
5491 NE2 HIS D 69
5491 NE2 HIS D 69
5492 C HIS D 69
5493 O HIS D 69
5493 O HIS D 69
5494 N SER D 70
5495 CA SER D 70
5495 CA SER D 70
5496 CB SER D 70
5497 OG SER D 70
5498 C SER D 70
5499 C SER D 70
5499 C SER D 70
5499 C SER D 70
5500 N PRO D 71
5501 CD PRO D 71
5501 CD PRO D 71
5502 CA PRO D 71
5503 CB PRO D 71
5504 CG PRO D 71
5505 C PRO D 71
5505 C PRO D 71
5506 CA ASP D 72
5507 N ASP D 72
5507 N ASP D 72
5508 CA ASP D 72
5509 CB ASP D 72
5511 CD ASP D 72
5510 CG ASP D 72
5510 CG ASP D 72
5511 CB GIN D 73
5512 CB GIN D 73
5522 C GIN D 73
5524 C GIN D 73
5524 C GIN D 73
5525 CA VAL D 74
5526 CB VAL D 74
5526 CB VAL D 74
5527 CG VAL D 74
5536 CA SER D 75
5536 CB PRO D 73
5530 CB SER D 73
5530 CB SER D 74
5524 CB CB CB VAL D 74
5526 CB VAL D 74
5526 CB VAL D 74
5526 CB VAL D 74
5536 CB SER D 75
5537 N SER D 73
5536 CB SER D 73
5537 N SER D 73
5538 CB SER D 73
5538 CB SER D 73
5539 CB SER D 73
5530 CB SER D 73
5531 N SER D 75
5531 N SER D 75
5532 CA SER D 75
5533 CB SER D 75
5534 CB SER D 73
5536 CB VAL D 74
5536 CB VAL D 74
5537 CB SER D 73
5538 CB SER D 73
5539 CB VAL D 74
5531 N SER D 75
5536 CA VAL D 74
5536 CA SER D 73
5537 CB SER D 73
5538 CB SER D 73
5539 CB SER D 73
5530 CB SER D 73
5531 N SER D 73
5531 N SER D 75
5532 CB VAL D 74
5531 N SER D 75
5533 CB SER D 75
5394 CG SER D 75
5394 CG SER D 73
5536 CA SER D 73
5537 CB SER D 73
5538 CB SER D 74
5531 N SER D 75
544 CB SER
                                                                                                                                                       40.012 79.707
39.328 80.655
                    MOTA
                                                                                                                                                                                                                                           3.157 1.00 80.32
                                                  5482 C
                    MOTA
                                                                                                                                                                                                                                          3.552 1.00 81.34
                                                                                         SER D 68
                   MOTA
                MOTA
                    MOTA
                    MOTA
                     MOTA
                     MOTA
10
                     MOTA
                     MOTA
                     MOTA
                      MOTA
                      MOTA
 15
                      MOTA
                      MOTA
                       MOTA
                       MOTA
                       MOTA
  20
                       MOTA
                                                                                                                                                                                                                                                                                                                                       7
                       MOTA
                        MOTA
                                                                                                                                                                                                                                                                                                                                       6
                         MOTA
                         MOTA
   25
                         MOTA
                         MOTA
                         MOTA
                          MOTA
                          MOTA
    30
                          ATOM
                                                                                                                                                                                                                                                                                                                                         б
                          MOTA
                          MOTA
                          MOTA
                           MOTA
     35
                                                                                                                                                                                                                                                                                                                                          7
                          MOTA
                           MOTA
                           MOTA
                           MOTA
                           ATOM
       40 ATOM
                             MOTA
                                                                                                                                                                                                                                                                                                                                            7
                             MOTA
                                                                                                                                                                                                                                                                                                                                              6
                             MOTA
                                                                                                                                                                                                                                                                                                                                              8
                             MOTA
                                                                                                                                                                                                                                                                                                                                              7
        45 ATOM
                              MOTA
                              MOTA

    42.087
    67.951
    10.973
    1.00
    48.36

    41.089
    67.959
    13.760
    1.00
    50.70

    42.240
    68.108
    14.173
    1.00
    49.32

    40.264
    67.023
    14.215
    1.00
    48.60

    40.696
    66.051
    15.206
    1.00
    46.92

                              MOTA
                                                                                                                                                                                                                                                                                                                                               6
                              MOTA
                                                                                                                                                                                                                                                                                                                                               6
         50 ATOM
                               MOTA
                               MOTA
                                                             5532 CA SER D 75
                                                                                                                                                                       39.555 65.729 16.166 1.00 48.45
39.444 66.718 17.168 1.00 48.28
41.159 64.789 14.487 1.00 44.70
40.397 64.143 13.781 1.00 43.70
                                MOTA
                                                            5533 CB SER D 75
5534 OG SER D 75
5535 C SER D 75
5536 O SER D 75
                                MOTA
          55 ATOM
                                MOTA
                                                              5537 N VAL D 76 42.424 64.449 14.675 1.00 43.70

5538 CA VAL D 76 43.024 63.281 14.039 1.00 43.43

5539 CB VAL D 76 44.283 63.687 13.264 1.00 44.79

5540 CG1 VAL D 76 44.891 62.486 12.604 1.00 43.63
                                 MOTA
                                 MOTA
                                 MOTA
           60
                                 MOTA
                                  MOTA
```

PCT/EP01/01457

						-103				_
	ATOM	5541	CG2	VAL D	76	43.943	64.746		1.00 42.10	6
	ATOM	5542	C	VAL D	76	43.419	62.193		1.00 43.50	6
		5543	ō	VAL D	76	44.004	62.472		1.00 45.44	8
	ATOM		14	PRO D	77	43.102	60.929		1.00 42.76	7
_	MOTA	5544		PRO D	77	42.235	60.402	13.656	1.00 41.52	6
5	MOTA	5545	CD		77	43.472		15.650	1.00 41.41	6
	MOTA	5546	CA	PRO D		42.856	58.628	15.009	1.00 42.36	6
	MOTA	5547	CB	PRO D	77		59.168	14.296	1.00 40.67	6
	MOTA	5548	CG	PRO D	77	41.674		15.749	1.00 40.15	6
	MOTA	5549	С	PRO D	77	44.985	59.774		1.00 39.02	8
10	MOTA	5550	0	PRO D	77	45.687	59.922	14.762	1.00 33.02	7
	MOTA	5551	N	ILE D	78	45.474	59.537	16.954		6
	ATOM	5552	CA	ILE D	78	46.899	59.421	17.217	1.00 42.23	
	MOTA	5553	CB	ILE D	78	47.113	59.019	18.687	1.00 43.04	6
	MOTA	5554		ILE D	78	48.495	58.518	18.924	1.00 45.01	6
15				ILE D		46.872	60.236	19.555	1.00 47.88	6
15	MOTA	5555		ILE D		47.618	61.461	19.057	1.00 48.43	6
	MOTA	5556				47.591	58.432	16.299	1.00 42.53	6
	MOTA	5557	C	ILE D		48.717	58.643	15.880	1.00 44.25	8
	MOTA	5558	0	ILE D			57.358	15.979	1.00 43.93	7
	ATOM	5559	N	SER D		46.891	56.302	15.127	1.00 43.22	6
20	ATOM	5560	CA	SER I		47.410			1.00 42.69	6
-	ATOM	5561	CB	SER I		46.457	55.110	15.185	1.00 43.59	8
	ATOM	5562	OG	SER I	79	45.130	55.523	14.910		6
	ATOM	5563	C	SER I		47.661	56.692	13.668	1.00 42.26	
	ATOM	5564	ō	SER I		48.319	55.953	12.937	1.00 41.56	8
05			N	SER I		47.138	57.835	13.243	1.00 39.86	7
25	MOTA	5565		SER I		47.326	58.282	11.871	1.00 40.25	6
	MOTA	5566	CA			46.026	58.840	11.307	1.00 40.77	6
	ATOM	5567	CB	SER I		45.025	57.845	11.259	1.00 48.70	8
	MOTA	5568	OG	SER I		48.413	59.342	11.742	1.00 41.01	6
	MOTA	5569	С	SER			59.842	10.655	1.00 41.05	8
30	MOTA	5570	0	SER		48.658		12.847	1.00 39.67	7
	ATOM	5571	N	LEU	D 81	49.067	59.671		1.00 39.96	6
	MOTA	5572	CA	LEU	D 81	50.112		12.844	1.00 40.31	6
	ATOM	5573	CB	LEU	D 81	49.703	61.886	13.684	1.00 42.96	6
	ATOM	5574		LEU	D 81	48.371	62.571	13.448	1.00 42.90	6
35		5575		1 LEU		48.019	63.429	14.638	1.00 41.75	
33	MOTA	5576	_	2 LEU		48.454	63.382	12.191	1.00 44.21	6
	MOTA			LEU		51.357	60.109	13.472	1.00 38.80	6
	MOTA	5577				51.303		14.119	1.00 39.28	8
	MOTA	5578		LEU		52.478		13.276	1.00 37.55	7
	MOTA	5579		TRP		53.726		13.891	1.00 36.02	6
40	MOTA	5580				54.927		13.158	1.00 39.06	6
	MOTA	5581	L CE					13.958	1.00 40.02	6
	ATOM	5582				56.206				6
	ATOM	5583	3 CI			56.71				6
	ATOM	5584		2 TRP	D 82	57.878				6 -
45	ATOM			E3 TRP	D 82	56.29		15.292		6
70	АТОМ			ol TRP	D 82	57.06		14.007		7
				E1 TRP		58.06	5 60.082	14.908	1.00 40.21	
	ATOM		, 1	Z2 TRP	D 82	58.63	0 61.997	16.422	1.00 36.80	6
	MOTA		0 0	Z3 TRP	D 82	57.03		16.247	1.00 40.18	6
	MOTA			H2 TRP	D 82	58.19		16.801	1.00 38.54	-6
50	MOTA					53.60			1.00 35.47	6
	MOTA			TRP		53.08				8
	ATOM	559	2 0				_			7
	ATOM	559	3 И			54.07				6
	ATOM	559	4 C	A VAL	D 83	53.99				6
55			5 C			52.82				6
	ATOM			G1 VAL		52.90				
	ATOM		7 0	G2 VAI	83 מי	51.50		0 17.83	2 1.00 35.92	٥
				_		55.33	5 60.81			6
	ATON					56.03				8
~	ATO					55.72			5 1.00 35.49	
60									4 1.00 37.20	6
	OTA	<u>v</u> 560	טון כ	D PRO	94 עי	55.0				

PCT/EP01/01457

						-164	C1 740	19.873	1.00 36.59	6
	MOTA	5602 C	A PRO			56.979	61.740		1.00 30.33	6
	MOTA	5603 C	B PRO	9 D 8	4	56.933	63.024	20.694	1.00 37.10	6
	MOTA	5604 C	G PRO	8 a c	4	56.196	63.930	19.835 20.759	1.00 35.92	6
	MOTA	5605 C	PRO	_	4	57.034	60.502	21.449	1.00 33.32	8
5	ATOM	5606 C) PRO		4	56.070	60.197	20.749	1.00 34.70	7
	MOTA	5607 N	N ASI		5	58.161	59.798	21.565	1.00 34.25	6
	MOTA	5608 C		_	5	58.283	58.609	20.925	1.00 35.35	6
	MOTA	5609 C			5	59.244	57.622 58.201	20.700	1.00 38.15	6
	MOTA			-	15	60.600	59.379	20.700	1.00 40.37	8
10	MOTA		OD1 AS	_	15	60.645	57.486	20.870	1.00 36.29	8
•	MOTA		OD2 AS	_	35	61.612 58.740	58.962	22.964	1.00 37.26	6
	MOTA		-		35	59.737	58.449	23.453	1.00 38.45	8
	MOTA			_	35	57.981	59.840	23.609	1.00 35.72	7
	MOTA			_	36	58.290	60.294	24.956	1.00 37.34	6
15	MOTA			_	36 36	57.397	61.471	25.325	1.00 35.58	6
	MOTA			_	36	57.576	62.690	24.434	1.00 36.77	6
	MOTA		CG LE		86	56.652	63.799	24.877	1.00 32.58	6
	MOTA		CD1 PE		86	59.026	63.127	24.496	1.00 36.92	6
00	MOTA			_	86	58.112	59.205	25.989	1.00 38.80	6
20	ATOM				86	57.250	58.337	25.853	1.00 43.05	8
	MOTA			_	87	58.925	59.263	27.033	1.00 38.29	7
	MOTA	5623 5624		LA D	87	58.852	58.291	28.103	1.00 38.34	6
	MOTA	5625		LA D	87	59.808	57.174	27.827	1.00 37.03	6
25	MOTA	5626		LA D	87	59.202	58.966	29.414	1.00 39.60	6
25	MOTA	5627	_	LA D	87	60.087	59.793	29.436	1.00 43.32	8 7
	MOTA MOTA	5628	_	LA D	88	58.495	58.644	30.492	1.00 39.86	, 6
	ATOM	5629		LA D	88	58.804	59.234	31.786	1.00 39.70	6
	ATOM	5630		LA D	88	57.572	59.294	32.654	1.00 38.81 1.00 41.02	6
30	ATOM	5631		LA D	88	59.861	58.347	32.418	1.00 41.02	8
00	ATOM	5632		LA D	88	59.575	57.259	32.894	1.00 42.74	7
	ATOM	5633	N T	YR D	89	61.095		32.400	1.00 44.50	6
	ATOM	5634		YR D	89	62.241				6
	MOTA	5635		YR D	89	63.443				6
35	MOTA	5636		YR D	89	63.940				6
	MOTA	5637		YR D	89	64.910				6
	MOTA	5638		YR D	89	65.384				6
	MOTA	5639		YR D	89	63.452 63.916				6
	MOTA	5640		ryr D	89	64.881				6
40	MOTA	5641		ryr D	89 89	65.343			3 1.00 61.62	8
	MOTA	5642		TYR D	89	62.04			1.00 43.55	6
	MOTA	5643		TYR D	89	62.61			3 1.00 43.31	8
	MOTA	5644	_	ASN D	90	61.26		2 35.173		7
45	MOTA	5645		ASN D	90	61.05	9 57.36			
45	MOTA	5646 5647		ASN D	90	61.45	9 58.32	3 37.60		
	MOTA			ASN D	90	60.71) 6
	MOTA			ASN D	90	60.60	2 60.27			8
	MOTA MOTA			ASN D	90	60.22				. 7 5 6
50				ASN D	90	59.64				8
50	MOTA		_	ASN D	90	59.17				1 7
	ATOM			ALA D	91	58.97				76
	ATOM			ALA D	91	-57.63			40 0	
	ATOM	·		ALA D	91 '	56.98				4 6
55				ALA D	91	57.82				0 8
-	ATOM			ALA D	91	58.71				8 7
	ATOM			ILE D		56.96				
	ATON		CA	ILE D		57.01				4 6
	OTA	4 5660		ILE D		56.83				
60	OTA C			ILE D	92	55.42 57.82				
	OTA	vi 5662	2 CG1	ILE D	92	57.0	, J2.J.	,		

							-165				_
	ATOM	5663	CD1	ILE D	92		57.559	52.447			6
	ATOM	5664	C	ILE D	92		55.921	51.998	37.180	1.00	6
	ATOM	5665	Ö	ILE D	92		55.867	50.816	37.502	1.00 43.77	8 7
	ATOM	5666	N	SER D	93		55.051	52.546	36.343	1.00 41.02	
5	ATOM	5667	CA	SER D			53.968	51.788	35.733	1.00 39.43	6 6
3	ATOM	5668	CB	SER D			52.673	51.994	36.498	1.00 40.39	
	ATOM	5669	OG	SER D			52.200	53.324	36.320	1.00 40.98	8
	ATOM	5670	C	SER D			53.802	52.387	34.366	1.00 39.82	6
		5671	0	SER D			54.349	53.452	34.103	1.00 38.78	8
10	MOTA	5672	N	LYS D			53.063	51.727	33.484	1.00 40.02	7
10	MOTA	5673	CA	LYS I			52.883	52.322	32.173	1.00 42.68	6
	ATOM ATOM	5674	CB	LYS I			52.695	51.260	31.081	1.00 42.12	6
		5675	CG	LYS I	· · · · · ·		51.789	50.113	31.405	1.00 45.31	6
	MOTA	5676	CD	LYS I			51.980	48.999	30.378	1.00 48.12	6
4 5	ATOM	5677	CE	LYS I			51.973	49.545	28.957	1.00 49.66	6
15	MOTA	5678	NZ	LYS			52.092	48.466	27.938	1.00 53.06	7
	MOTA		C	LYS !			51.738	53.319	32.205	1.00 42.30	6
	MOTA	5679	0	LYS			50.899	53.299	33.104	1.00 42.15	8
	MOTA	5680		PRO 1			51.707	54.230	31.234	1.00 41.20	7
00	MOTA	5681	И	PRO			52.637	54.379	.30.108	1.00 37.85	6
20	ATOM	5682	CD CA	PRO			50.655	55.243	31.178	1.00 40.86	6
	MOTA	5683	CB	PRO			51.064	56.117	29.990	1.00 41.55	6
	MOTA	5684	CG	PRO			52.512	55.834	29.821	1.00 42.69	6
	MOTA	5685		PRO			49.263	54.691	30.981	1.00 39.96	6
0.5	MOTA	5686	C	PRO			49.030	53.893	30.080	1.00 39.70	8
25	ATOM	5687		GLU	_		48.344	55.113	31.835	1.00 40.14	7
	ATOM	5688			_		46.961	54.718	31.689	1.00 38.41	6
	ATOM	5689					46.321		33.041	1.00 40.63	6
	MOTA	5690					44.880		32.923	1.00 48.74	6
-00	MOTA	5691			_		44.232		34.273	1.00 51.27	6
30	MOTA	5692		1 GLU			44.983		35.261	1.00 50.19	8
	MOTA	5693		2 GLU		6	42.979		34.345	1.00 50.07	8
	MOTA	5694		GLU		6	46.324		31.084	1.00 37.34	6
	MOTA	5695		GLU		6	45.998		31.799	1.00 36.63	8
	MOTA	5690		VAL		7	46.199		29.760	1.00 34.71	7
35	MOTA	569				7	45.599		29.079	1.00 32.69	6
	MOTA	569				97	45.881			1.00 30.58	6
•	MOTA	569		3 VAL		7	45.289		26.896	1.00 30.36	6
	MOTA			G2 VAL		97	47.363		7 27.354	1.00 28.89	6
	MOTA		-	VAL کی VAL		97	44.10			1.00 34.47	6
40						97	43.43		28.962	1.00 35.88	8
	MOTA					98	43.59		1 30.019	1.00 35.68	7
	MOTA					98	42.19		4 30.40	1.00 36.36	6
	MOTA	_			_	98	42.07			3 1.00 35.92	6
	ATOM		-		_	98	42.94		7 32.89		6
45				G LEU	, –	98	42.90			4 1.00 35.58	6
	ATOM			D1 LEU	_	98	42.45			7 1.00 39.84	6
	ATOM	_		D2 LEU		98	41.27			6 1.00 38.24	6
	MOTA				_	98	40.05	_		9 1.00 37.04	8
	ATOM				JD	99	41.86			8 1.00 37.00	7
50					R D		41.08	_		4 1.00 36.28	6
	MOTA				R D	99	41.44			8 1.00 36.19	6
	ATO				R D	99	42.86			7 1.00 38.29	8
	ATO			OG1 TH	K D	99	41.07			6 1.00 31.31	. 6
	ATO			CG2 TH		99	41.22			.0 1.00 35.89	6
55	5 ATO				R D	99	42.14			8 1.00 35.45	8
	ATO:			O TH	R D	99	40.2	-		34 1.00 34.88	7
	OTA			N PR	O D :	100				37 1.00 35.25	6
	OTA			CD PR	O D 3	100	40.3			31 1.00 33.36	6
	ATO			_	G 03	100	39.2		92 23.02	24 1.00 32.41	
6	OTA 0			CB PF	OD:	100	38.2				
	ATC	M 57	23	CG PF	O D	T00	JU.2		-		

	0 01,00								
				:	-166				
	N/OW	5724	C	PRO D 100	41.666	59.955	23.077	1.00 35.04	6
	MOTA			PRO D 100	42.188		23.310	1.00 36.02	8
	ATOM	5725		GLN D 101	42.256		22.350	1.00 38.56	7
	ATOM	5726			43.574			1.00 39.66	6
_	ATOM	5727		GLN D 101	44.356			1.00 38.98	6
5	MOTA	5728		GLN D 101				1.00 41.80	6
	MOTA	5729		GLN D 101	44.890			1.00 46.38	6
	ATOM	5730		GLN D 101	45.318			1.00 50.42	8
	ATOM	5731		GLN D 101	46.158			1.00 49.13	7
•	ATOM	5732	NE2	GLN D 101	44.735	55.447			6
10	MOTA	5733	С	GLN D 101	43.543	59.994		1.00 39.27	
	ATOM	5734	0	GLN D 101	43.965	59.463	-	1.00 38.19	8
	ATOM	5735	N	LEU D 102	43.037	61.224		1.00 40.46	7
	ATOM	5736	CA	LEU D 102	42.910	62.103	19.381	1.00 40.51	6
			CB	LEU D 102	41.467	62.590	19.231	1.00 37.39	6
4 5	ATOM	5737		LEU D 102	40.382	61.515	19.121	1.00 38.97	6
15	MOTA	5738	CG	LEU D 102	39.030	62.182	18.988	1.00 36.48	6
	MOTA	5739			40.657	60.628	17.925	1.00 36.34	6
	MOTA	5740		LEU D 102	43.804	63.308	19.554	1.00 41.42	6
	MOTA	5741	С	LEU D 102		63.794	20.665	1.00 43.09	8
	MOTA	5742	0	LEU D 102	43.990		18.455	1.00 40.44	7
20	ATOM	5743	N	ALA D 103	44.375	63.777	18.489	1.00 40.53	6
	MOTA	5744	CA	ALA D 103	45.221	64.953		1.00 43.43	6
	MOTA	5745	CB	ALA D 103	46.549	64.673	17.847	1.00 41.82	6
	MOTA	5746	С	ALA D 103	44.500	66.050	17.731	1.00 41.33	8
	ATOM	5747	0	ALA D 103	43.503	65.803	17.058		7
25	MOTA	5748	N	ARG D 104	44.998	67.271	17.849	1.00 42.58	
20	MOTA	5749	CA	ARG D 104	44.369	68.381	17.165	1.00 43.20	6
		5750	CB	ARG D 104	43.995	69.450	18.183	1.00 43.57	6
	MOTA		CG	ARG D 104	43.032	70.480	17.678	1.00 40.98	6
	MOTA	5751		ARG D 104	41.674	69.900	17.425	1.00 39.96	6
-00	MOTA	5752	CD	ARG D 104	40.803		16.909	1.00 41.32	7
30	MOTA	5753	NE	ARG D 104 ARG D 104	39.517		16.635	1.00 39.52	6
	MOTA	5754		ARG D 104	38.927		16.824	1.00 40.96	7
	MOTA	5755	_	ARG D 104	38.826		16.175	1.00 38.44	7
	MOTA	5756		2 ARG D 104			16.162	1.00 43.89	6
	MOTA	5757		ARG D 104	45.380		16.526	1.00 44.97	8
35	MOTA	5758	0	ARG D 104	46.508		14.894	1.00 44.88	7
	MOTA	5759	N	VAL D 105	44.989	_	13.863	1.00 46.87	6
	MOTA	5760	CA	VAL D 105	45.910		12.751	1.00 44.91	໌ 6
	MOTA	5761	СВ	VAL D 105	46.094	68.380		1.00 42.60	6
	MOTA	5762	CG:	1 VAL D 105	47.165		11.787	1.00 43.58	· 6
40	ATOM	5763	CG:	2 VAL D 105	46.469		13.346		6
70	MOTA	5764		VAL D 105	45.46		13.223	1.00 48.29	
		5765		VAL D 105	44.33	5 70.845	12.731	1.00 47.85	8
	MOTA	576		VAL D 106	46.37	5 71.702	13.238	1.00 48.47	7
	MOTA		-		46.12		12.663	1.00 50.73	6
	ATOM	500			46.85		13.472	1.00 50.55	6
45	MOTA			1 VAL D 106	46.39			1.00 51.23	6
	ATOM			O 1771 D 106	46.60			1.00 48.01	6
	MOTA			2 VAL D 106	46.63				6
	ATOM			VAL D 106					8
	ATOM	577	2 0	VAL D 106	47.66				7
50	ATOM	577	3 N	SER D 107	45.92				6
_	ATOM		4 CF		46.28				6
	ATOM		5 CF	3 SER D 107	45.39		8.185		8
	ATOM			- 400	45.25				
	ATOM			SER D 107	47.72	6 74.058			6
55				SER D 107	48.18	8 73.739		- -	
55		-		ASP D 108	48.45				7
	ATON			400			9,262	1.00 57.12	
	ATON							5 1.00 58.24	
	ATO		_	B ASP D 100				5 1.00 61.04	. 6
	IOTA		32 C	G ASP D 108					8
60				D1 ASP D 108					
	MOTA	<u>4</u> 578	34 O	D2 ASP D 108	51.10	,,,,,,			

,	WO 01/58	951				1.7			PCT/EP01/014	57
	ATOM	5785	С	ASP D	108	-167 50.827	73.870	9.665	1.00 58.88	6
	ATOM	5786		ASP D		52.043	74.071	9.635	1.00 61.62	8 .
	ATOM	5787		GLY D		50.293	72.711	10.051	1.00 58.94	7
	MOTA	5788	CA	GLY D	109	51.134	71.589	10.437	1.00 58.18	6
5	MOTA	5789		GLY D		51.424	71.483	11.918	1.00 57.62	6
	MOTA	5790		GLY D		52.186	70.612	12.343	1.00 56.21	8 7
	MOTA	5791		GLU D		50.831	72.370	12.707	1.00 58.61 1.00 59.21	6
	MOTA	5792	CA	GLU D		51.042 50.664	72.345 73.700	14.152 14.776	1.00 53.21	6
10	MOTA	5793	CB	GLU D		51.327	74.002	16.134	1.00 66.58	6
10	ATOM ATOM	5794 5795	CG CD	GLU D		52.852	74.104	16.041	1.00 69.79	6
	MOTA	5796		GLU D		53.375	74.340	14.921	1.00 70.58	8
	ATOM	5797		GLU D		53.527	73.963	17.089	1.00 70.10	8
	ATOM	5798	C	GLU D		50.158	71.232	14.712	1.00 56.76	6
15	MOTA	5799	Ō	GLU D	110	49.001	71.079	14.320	1.00 54.86	8
	MOTA	5800	N	VAL D		50.723	70.451	15.625	1.00 55.23	7
	MOTA	5801	CA	VAL D		50.013	69.333	16.236	1.00 53.43	6 6
	MOTA	5802	СВ	VAL D		50.704	67.976	15.889	1.00 53.47 1.00 51.83	6
00	ATOM	5803		VAL D		49.934	66.821	16.500 14.382	1.00 52.57	6
20	MOTA	5804		VAL D		50.798 49.962	67.803 69.470	17.754	1.00 53.05	6
	ATOM	5805 5806	C	VAL D		50.972	69.747	18.400	1.00 52.81	8
	ATOM ATOM	5807	N O	LEU D		48.783	69.269	18.323	1.00 51.91	7
	MOTA	5808	CA	LEU D		48.631	69.354	19.766	1.00 51.71	6
25	ATOM	5809	CB	LEU D		47.776	70.566	20.155	1.00 55.12	6
	ATOM	5810	CG	LEU D	112	47.832	71.901	19.392	1.00 55.82	6
	MOTA	5811		LEU D		49.269	72.287	19.035	1.00 56.65	6
	MOTA	5812	CD2	LEU D		46.985	71.777	18.155	1.00 55.54	6
	MOTA	5813	С	LEU D		47.959	68.089	20.292	1.00 51.46 1.00 51.33	6 8
30	ATOM	5814	0	LEU D		46.833	67.769	19.900 21.162	1.00 31.33	7
	MOTA	5815	N	TYR D		48.659 48.128	67.365 66.149	21.762	1.00 45.71	6
	ATOM	5816	CA	TYR D		48.941	64.928	21.318	1.00 43.52	6
	MOTA	5817 5818	CB CG	TYR D		48.490	63.601	21.918	1.00 41.37	6
35	ATOM ATOM	5819		TYR D		47.142	63.255	21.975	1.00 39.60	6
00	MOTA	5820	CE1	TYR D	113	46.735	62.028	22.492	1.00 38.43	6
	ATOM	5821		TYR D		49.423	62.679	22.397	1.00 40.11	6
	MOTA	5822	CE2	TYR D		49.028	61.458	22.911	1.00 39.17	6
	MOTA	5823	CZ	TYR I		47.682	61.134	22.958	1.00 40.31 1.00 40.08	6 8
40	MOTA	5824	OH	TYR I		47.283	59.921	23.470 23.262	1.00 45.22	6
	ATOM	5825	С	TYR I		48.218 49.302	66.325 66.442	23.202	1.00 44.34	8
	ATOM	5826	0	TYR I		47.073	66.352	23.924	1.00 47.16	7
	ATOM	5827	N	MET I		47.073			1.00 48.56	6
45	ATOM ATOM	5828 5829		MET I	114	46.457	67.906	25.681	1.00 53.17	6
70	ATOM	5830		MET I		46.536	68.281	27.130	1.00 58.47	6
	ATOM	5831		MET I		45.470	69.687	27.429	1.00 64.86	16
	MOTA	5832		MET I		46.527	70.991	26.840	1.00 63.87	6
	ATOM	5833	C	MET I		46.214	65.472	26.062	1.00 47.72 1.00 47.31	6
50	MOTA	5834		MET I		45.060	65.705	26.424	_	8 7
	MOTA	5835			115	46.790		26.251 25.761		6
	ATOM	5836			115	48.108 46.080				6
	MOTA	5837			0 115 0 115	46.818				6
55	MOTA	5838 5839			0 115	48.231				6
55	MOTA MOTA	5840			D 115	46.159			1.00 44.40	6
	MOTA	5841			115	47.145				8
	ATOM	5842		SER	D 116	45.124				7
	MOTA	5843			D 116	45.142				6 6
60	MOTA	5844			D 116	43.752		_		8
	MOTA	5845	5 OG	SER	D 116	43.829	63.015	32.516	T.00 44.3/	J

PCT/EP01/01457

5906

MOTA

С

WO 01/58951

-168 45.712 61.484 30.957 1.00 42.16 SER D 116 5846 C MOTA 45.190 60.448 30.569 1.00 45.67 SER D 116 5847 O MOTA 46.781 61.493 31.739 1.00 39.79 ILE D 117 5848 N MOTA MOTA 5849 5 5850 MOTA 5851 MOTA 6 5852 MOTA 6 MOTA 5853 6 5854 MOTA 8 10 MOTA 5855 5856 MOTA 6 5857 MOTA 6 5858 MOTA 6 MOTA 5859 6 15 5860 MOTA 5861 АТОМ 6 5862 MOTA 7 5863 MOTA 7 MOTA 5864 6 20 5865 MOTA MOTA 5866 O MOTA 5867 N 6 5868 CA MOTA ATOM 5869 34.807 1.00 39.00 33.476 1.00 37.41 5870 CG GLN D 119 52.879 56.638 34.807 1.00 39.00 5871 CD GLN D 119 53.483 57.037 33.476 1.00 37.41 5872 OE1 GLN D 119 53.349 58.169 33.043 1.00 42.14 5873 NE2 GLN D 119 54.154 56.112 32.831 1.00 38.80 5874 C GLN D 119 51.491 56.961 37.534 1.00 42.32 5875 O GLN D 119 51.421 57.965 38.213 1.00 43.53 5876 N ARG D 120 52.197 55.908 37.906 1.00 43.85 5877 CA ARG D 120 52.950 55.944 39.149 1.00 47.43 5878 CB ARG D 120 52.819 54.632 39.900 1.00 50.39 5879 CG ARG D 120 51.389 54.278 40.235 1.00 58.64 < 34.807 52.879 56.638 GLN D 119 25 MOTA MOTA MOTA 7 MOTA 6 MOTA 8 30 MOTA 7 MOTA MOTA 5881 NE ARG D 120 51.352 53.441 41.493 1.00 64.21 5882 CZ ARG D 120 52.129 53.942 43.790 1.00 65.70 64.48 NH1 ARG D 120 52.911 52.870 43.763 1.00 64.48 5884 NH2 ARG D 120 52.049 54.678 44.895 1.00 62.69 5885 C ARG D 120 54.411 56.231 38.913 1.00 46.83 5886 O ARG D 120 54.969 55.848 37.885 1.00 46.53 5887 N PHE D 121 55.032 56.912 39.869 1.00 45.77 5888 CA PHE D 121 56.443 57.249 39.743 1.00 45.26 5890 CB PHE D 121 56.627 58.737 39.416 1.00 42.47 5890 CG PHE D 121 55.893 59.186 38.199 1.00 41.19 5891 CD1 PHE D 121 54.546 59.483 38.266 1.00 39.80 5893 CE1 PHE D 121 56.544 59.284 36.979 1.00 39.10 5893 CE1 PHE D 121 55.862 59.670 35.858 1.00 37.48 5895 CZ PHE D 121 55.862 59.670 35.858 1.00 37.48 5895 CZ PHE D 121 54.512 59.965 35.937 1.00 38.89 MOTA MOTA 35 MOTA MOTA MOTA 7 MOTA 7 MOTA 6 MOTA 40 8 MOTA 7 MOTA MOTA 6 MOTA 6 45 MOTA 6 MOTA 6 MOTA MOTA 59.670 35.858 1.00 37.48 MOTA 6 50 MOTA 6 MOTA 56.783 42.077 56.881 40.769 1.00 43.10 8 PHE D 121 56.729 MOTA 5897 0 1.00 48.75 7 58.560 SER D 122 5898 N MOTA 56.672 41.837 1.00 51.22 6 SER D 122 59.520 5899 CA MOTA 1.00 51.58 55.604 41.442 60.535 SER D 122 55 5900 CB MOTA 1.00 51.33 55.455 42.453 61.510 SER D 122 5901 OG MOTA 1.00 51.78 60.224 58.027 42.004 SER D 122 5902 С MOTA 60.968 58.460 41.123 1.00 50.44 59.965 58.699 43.120 1.00 52.36 SER D 122 60.968 58.460 41.123 1.00 50.44 CYS D 123 59.965 58.699 43.120 1.00 52.36 CYS D 123 60.564 59.999 43.370 1.00 55.03 CYS D 123 60.584 60.314 44.860 1.00 57.50 5903 0 MOTA 5904 N MOTA 6 CYS D 123 60 MOTA 5905 CA

PCT/EP01/01457

| September | Sept WO 01/58951 -169 MOTA MOTA MOTA MOTA MOTA MOTA MOTA MOTA ATOM 10 ATOM ATOM MOTA MOTA MOTA 15 MOTA MOTA MOTA MOTA MOTA 20 MOTA MOTA ATOM MOTA MOTA 25 MOTA MOTA MOTA MOTA MOTA 30 MOTA MOTA MOTA MOTA ATOM 35 MOTA 7 MOTA MOTA 6 MOTA MOTA 40 ATOM 8 MOTA 6 MOTA 8 MOTA 7 ATOM 6 45 MOTA 6 MOTA MOTA 6 MOTA MOTA 50 MOTA 7 MOTA б ATOM 6 MOTA 6 MOTA 55 MOTA MOTA MOTA MOTA 8 MOTA 60 MOTA

MOTA

ATOM 5969 OG SER D 132 59.812 7 ATOM 5970 C SER D 132 57.316 7	71.733 71.551 71.530 70.575 69.406	52.788 53.401 51.753 50.563 52.337	1.00 75.96 1.00 76.36 1.00 72.89	6 8
ATOM 5969 OG SER D 132 59.812 7 ATOM 5970 C SER D 132 57.316 7	71.733 71.551 71.530 70.575 69.406	53.401 51.753 50.563	1.00 76.36 1.00 72.89	8
ATOM 5970 C SER D 132 57.316 7	71.551 71.530 70.575 69.406	51.753 50.563	1.00 72.89	
	71.530 70.575 69.406	50.563		
	70.575 69.406			6
111011 05/12 0 0211 0 000	69.406	50 337	1.00 73.06	8
0 111011 05.12 11 02.1 - 0-1			1.00 70.56	7 6
	00.04/	51.599 50.917	1.00 67.95 1.00 66.74	6
111011 05/1 0 000- 0 000-		51.257	1.00 65.57	8
		49.942	1.00 65.62	7
		49.194	1.00 63.00	6
10 111011 5577 611 1	-	49.145	1.00 62.05	6
	67.597	47.785	1,00 60.69	6
	68.357	47.298	1.00 57.71	8
ATOM 5981 N THR D 135 59.149	67.206	47.139	1.00 60.08	7
O Alon 5502 CH Cim =	67.619	45.777	1.00 59.14	6
A10M 3303 CD 11M 2 222	68.590	45.703	1.00 59.67	6
Alon 5501 002 11m 2 20	69.735	46.516	1.00 62.19 1.00 57.77	8 6
A1011 3303 CO2 2111 2 105	69.031	44.263 44.963	1.00 57.77	6
A10N 3300 C 1 =	66.387 65.804	45.065	1.00 56.51	8
ZO AIOM Sydy O Time 2 100	65.995	44.170	1.00 56.67	7
AION 5500 N CID 2 200	64.836	43.314	1.00 55.02	6
	65.310	41.906	1.00 55.53	6
MIGHT SSSC C CCC	66.060	41.282	1.00 53.64	8
	64.115	43.347	1.00 55.35	6
ATOM 5993 SG CYS D 136 57.280	62.756	42.175	•	16
AION 5554 IV INC 2 20	64.889	41.414	1.00 55.15	7
AIOM JJJJ CA IIIO B IV	65.291	40.084	1.00 56.13 1.00 59.85	6 6
AIOM 5550 CB IMC 2 22	65.664	40.080 40.993	1.00 59.85	6
00 A10H 5557 CG 12C 2	66.818 66.718	41.445	1.00 67.87	6
ATOM 5550 CB 1110 2 127	67.425	42.706	1.00 72.81	7
AIOM 3333 NE INC 2 137	68.753	42.848	1.00 76.15	6
ATOM 6000 CZ ARG D 137 64.221 ATOM 6001 NH1 ARG D 137 63.975	69.545	41.798	1.00 76.59	7
35 ATOM 6002 NH2 ARG D 137 64.408	69.295	44.051	1.00 75.96	7
ATOM 6003 C ARG D 137 60.511	64.156	39.112	1.00 54.79	6
ATOM 6004 O ARG D 137 60.844	63.011	39.394	1.00 55.64	8
ATOM 6005 N ILE D 138 59.935	64.498	37.966	1.00 52.46	7
ATOM 6006 CA ILE D 138 59.618	63.551	36.923	1.00 49.86 1.00 47.60	6 6
40 ATOM 6007 CB ILE D 138 58.092	63.516	36.686	1.00 47.60	6
ATOM 6008 CG2 ILE D 138 57.769	62.562 63.120	35.565 37.975	1.00 44.38	6
ATOM 6009 CG1 ILE D 138 57.368 ATOM 6010 CD1 ILE D 138 55.873	63.120	37.903	1.00 39.29	6
100 (0.707	64.004	35.645	1.00 50.53	6
ATOM 6011 C ILE D 138 60.307 45 ATOM 6012 O ILE D 138 60.056	65.103	35,163	1.00 47.86	8
ATOM 6013 N LYS D 139 61.171	63.158	35.093	1.00 52.17	7
ATOM 6014 CA LYS D 139 61.881	63.497	33.857	1.00 53.46	6
ATOM 6015 CB LYS D 139 63.381	63.195	33.988	1.00 54.96	6
ATOM 6016 CG LYS D 139 64.040	63.838	35.187	1.00 59.06	6
50 ATOM 6017 CD LYS D 139 65.558	63.761	35.119	1.00 60.55 1.00 62.84	6 6
ATOM 6018 CE LYS D 139 66.116	64.685	34.044	1.00 62.84	7
ATOM 6019 NZ LYS D 139 67.604	64.584	33.930 32.667	1.00 52.45	6
ATOM 6020 C LYS D 139 .61.335 ATOM 6021 O LYS D 139 61.269	62.715 61.493	32.708	1.00 52.48	8
Alon out o alo -	63.411	31.604	1.00 51.17	7
00 11011 0022 1,	62.723	30.426	1.00 51.40	6
ATOM 6023 CA ILE D 140 60.453 ATOM 6024 CB ILE D 140 58.886	62.781	30.369	1.00 52.71	6
ATOM 6025 CG2 ILE D 140 58.303	62.478	31.748	1.00 53.74	6
ATOM 6026 CG1 ILE D 140 58.387	64.171	30.003	1.00 52.18	6
60 ATOM 6027 CD1 ILE D 140 56.892	64.354	30.322	1.00 51.22	6
ATOM 6028 C ILE D 140 61.078	63.251	29.123	1.00 50.75	6

•	W O 01/362	31						101/2101/01/0	•
					-171				
	ATOM	6029	0	ILE D 140	61.189	64.451	28.918	1.00 50.51	8
	MOTA	6030	N	GLY D 141	61.511	62.340	28.258	1.00 48.91	7
	MOTA	6031	CA	GLY D 141	62.112	62.735	26.997	1.00 48.03	6
	ATOM	6032	C	GLY D 141	62.036	61.611	25.983	1.00 47.81	6
5	ATOM	6033	0	GLY D 141	61.636	60.511	26.340	1.00 50.42	8
5					62.405	61.865	24.729	1.00 45.08	7
	MOTA	6034	N	SER D 142	62.364	60.824	23.713	1.00 42.21	6
	ATOM	6035	CA	SER D 142		61.334	22.376	1.00 43.40	6
	MOTA	6036	СВ	SER D 142	62.872			1.00 43.40	8
4.0	MOTA	6037	OG	SER D 142	63.079	60.255	21.482		6
10	MOTA	6038	С	SER D 142	63.194	59.630	24.126	1.00 44.37	8
	MOTA	6039	0	SER D 142	64.284	59.758	24.688	1.00 45.99	
	ATOM	6040	N	TRP D 143	62.673	58.452	23.825	1.00 46.12	7
	ATOM	6041	CA.	TRP D 143	63.338	57.222	24.196	1.00 45.24	6
	MOTA	6042	СВ	TRP D 143	62.300	56.121	24.425	1.00 42.93	6
15	MOTA	6043	CG	TRP D 143	62.872	54.893	25.051	1.00 39.90	6
	ATOM	6044	CD2	TRP D 143	63.244	54.737	26.418	1.00 37.42	6
	ATOM	6045	CE2	TRP D 143	63.740	53.425	26.567	1.00 37.64	6
	MOTA	6046	CE3		63.204	55.581	27.536	1.00 35.75	6
	ATOM	6047		TRP D 143	63.154	53.702	24.436	1.00 40.17	6
20	ATOM	6048		TRP D 143	63.676	52.817	25.341	1.00 38.55	7
20	ATOM	6049		TRP D 143	64.187	52.935	27.788	1.00 38.02	6
		6050		TRP D 143	63.647	55.100	28.741	1.00 36.62	6
	MOTA		CH2		64.133	53.784	28.863	1.00 39.07	6
	MOTA	6051		TRP D 143	64.348	56.758	23.170	1.00 46.24	6
05	MOTA	6052	C	TRP D 143	65.328	56.109	23.509	1.00 48.11	8
25	MOTA	6053	0		64.124	57.080	21.910	1.00 45.62	7
	MOTA	6054	N	THR D 144	65.047	56,616	20.894	1.00 44.68	6
	MOTA	6055	CA	THR D 144			19.955	1.00 44.87	6
	MOTA	6056	CB	THR D 144	64.336	55.633		1.00 41.93	8
	MOTA	6057	OG1		63.155	56,242	19.421	1.00 44.03	6
30	MOTA	6058	CG2		63.931	54.394	20.720	1.00 46.21	6
	ATOM	6059	C	THR D 144	65.703	57.710	20.075	1.00 40.21	8
	MOTA	6060	0	THR D 144	66.662	57.452	19.366	1.00 47.29	
	MOTA	6061	N	HIS D 145	65.198	58.931	20.173	1.00 47.13	7
	ATOM	6062	CA	HIS D 145	65.772	60.021	19.403	1.00 50.18	6
35	ATOM	6063	CB	HIS D 145	64.672	60.793	18.679	1.00 50.55	6
	ATOM	6064	CG	HIS D 145	63.961	59.997	17.630	1.00 52.45	6
	MOTA	6065	CD2	HIS D 145	64.369	59.558	16.416	1.00 51.92	6
	ATOM	6066	ND1	. HIS D 145	62.652	59.589	17.765	1.00 50.59	7
	MOTA	6067		HIS D 145	62.282	58.936	16.679	1.00 51.27	6
40	ATOM	6068		HIS D 145	63.305	58.902	15.844	1.00 52.81	7
. •	MOTA	6069		HIS D 145	66.611	60.990	20.241	1.00 52.96	6
	MOTA	6070		HIS D 145	66.147	61.554	21.236	1.00 51.74	8
	MOTA	6071		HIS D 146	67.856	61.179	19.828	1.00 53.81	7
	MOTA	6072		HIS D 146	68.748	62.081	20.532	1.00 55.05	6
45		6072		HIS D 146			20.267	1.00 53.71	6
40	ATOM			HIS D 146	70.555	61.617	18.816	1.00 52.77	6
	MOTA	6074	CG	2 HIS D 146	70.425	62.526	17.821	1.00 53.89	6
	MOTA	6075		1 HIS D 146	71.083	60.487	18.236	1.00 49.45	7
	MOTA	6076			71.261	60.700	16.945	1.00 49.76	6
	MOTA	6077		HIS D 146		61.929	16.667	1.00 51.93	7
50	MOTA	6078		2 HIS D 146	70.869	63.521	20.094	1.00 56.51	6
	MOTA	6079		HIS D 146	68.489		19.185	1.00 58.53	8
	MOTA	6080		HIS D 146	67.682	63.770		1.00 57.97	7
	MOTA	6081	. N	SER D 147	.69.190	64.455	20.738	1.00 58.69	6
	MOTA	6082	CA		69.054		20.497		
55	MOTA	6083	CB		70.097		21.332	1.00 58.36	6
	MOTA	6084	4 OG		71.365		21.179	1.00 58.90	8
	MOTA	6085	5 C	SER D 147			19.049		6
	MOTA	6086	5 0	SER D 147			18.727		8
	ATOM	6087		ARG D 148	69.768		18.180		7
60	ATOM	6088					16.790		6
	MOTA	6089			71.054	65.340	16.126	1.00 64.67	6

60

MOTA MOTA

PCT/EP01/01457 WO 01/58951 -172 MOTA MOTA MOTA MOTA 5 MOTA MOTA ATOM MOTA MOTA 10 ATOM ATOM MOTA MOTA MOTA 15 MOTA MOTA MOTA MOTA MOTA 20 MOTA MOTA МОТА MOTA MOTA 25 MOTA MOTA MOTA MOTA MOTA 30 ATOM MOTA MOTA ATOM ATOM 35 атом MOTA MOTA MOTA MOTA 40 ATOM MOTA MOTA MOTA MOTA 45 ATOM MOTA MOTA MOTA MOTA 50 MOTA MOTA MOTA MOTA MOTA 55 ATOM MOTA MOTA MOTA MOTA

	WO 01/589	951							PCT/EP01/0145	57
						-173		00 505		_
	ATOM	6151 6152	CA CB	THR D		53.911 52.372	78.559 78.483	29.705 29.424	1.00 93.25 1.00 94.48	6 6
	MOTA MOTA	6153		THR D		52.372	78.485	28.019	1.00 94.40	8
	MOTA	6154		THR D		51.619	79.546	30.255	1.00 93.74	6
5	MOTA	6155	C	THR D		54.104	78.445	31.220	1.00 94.44	6
	MOTA	6156	0	THR D	156	53.471	77.615	31.898	1.00 93.56	8
	MOTA	6157	N	GLU D		54.955	79.314	31.750	1.00 96.79	7
	MOTA	6158	CA	GLU D		55.252	79.320	33.183 33.416	1.00 99.37	6
10	MOTA	6159 6160	CB	GLU D		56.670 57.701	79.865 79.333	32.426	1.00100.34 1.00102.84	6 6
10	MOTA MOTA	6161	CG CD	GLU D		59.086	79.955	32.629	1.00102.04	6
	ATOM	6162		GLU D		59.179	81.213	32.700	1.00104.68	8
	MOTA	6163	OE2			60.085	79.189	32.707	1.00105.54	8
	MOTA	6164	С	GLU D	157	54.237	80.165	33.967	1.00 99.49	6
15	MOTA	6165	0	GLU D		54.273	80.216	35.210	1.00100.21	8
	ATOM	6166	N	ASN D		53.336	80.828	33.248	1.00 98.56	7 6
	MOTA	6167	CA	ASN D		52.340 51.632	81.657 82.550	33.911 32.894	1.00 98.16 1.00100.26	6
	ATOM ATOM	6168 6169	CB CG	ASN D		52.610	83.378	32.064	1.00103.20	6
20	MOTA	6170		ASN D		53.425	84.153	32.607	1.00101.77	8
	MOTA	6171		ASN D		52.533	83.221	30.735	1.00102.21	7
	MOTA	6172	С	ASN D		51.313	80.786	34.613	1.00 96.52	6
	MOTA	6173	0	ASN D		51.475	80.452	35.797	1.00 96.76	8
OF	MOTA	6174	N	SER D		50.257	80.447 79.599	33.864 34.313	1.00 94.02 1.00 90.18	7 6
25	MOTA	6175	CA	SER D		49.142 48.996	78.422	33.331	1.00 90.15	6
	MOTA MOTA	6176 6177	CB OG	SER I		50.277	77.932	32.940	1.00 90.19	8
	ATOM	6178	C	SER I		49.254	79.071	35.751	1.00 87.40	6
	ATOM	6179	ō	SER D		50.208	78.372	36.094	1.00 87.99	8
30	MOTA	6180	N	ASP I		48.282	79.408	36.594	1.00 83.57	7
	MOTA	6181	CA	ASP I		48.300	78.947	37.984	1.00 79.69	6
	MOTA	6182	CB	ASP I		46.950	79.189 78.632	38.660 40.079	1.00 79.26 1.00 79.02	6 6
	MOTA	6183 6184	CG OD1	ASP I		46.902 45.785	78.385	40.596	1.00 78.94	8
35	ATOM ATOM	6185		ASP I		47.987	78.446	40.679	1.00 77.43	8
00	ATOM	6186	C	ASP I		48.579	77.453	37.995	1.00 77.55	6
	MOTA	6187	0	ASP I	160	47.797	76.670	37.429	1.00 77.70	8
	ATOM	6188	N	ASP I		49.676	77.062	38.646	1.00 74.02	7
40	MOTA	6189	CA	ASP I		50.070	75.657	38.719	1.00 69.51 1.00 68.24	6 6
40	MOTA	6190	CB	ASP I		51.277 52.556	75.466 76.004	39.642 39.050	1.00 67.15	6
	MOTA MOTA	.6191 6192	CG OD1	ASP I		52.734	75.886	37.827	1.00 67.47	8
	ATOM	6193		ASP I		53.397	76.536	39.803	1.00 70.25	8
	MOTA	6194	C	ASP I		48.972	74.697	39.147	1.00 67.31	6
45	MOTA	6195	0	ASP I	161	49.071	73.497	38.890	1.00 68.61	8
•	ATOM	6196	N		162	47.924	75.191	39.788	1.00 64.39	7
	ATOM	6197	CA		162	46.871	74.280	40.210 41.736	1.00 63.54 1.00 63.26	6 6
	ATOM	6198	CB		162 162	46.897 46.555	74.097 75.286	42.417	1.00 65.64	8
50	MOTA ATOM	6199 6200	OG C		0 162	45.494	74.722	39.761	1.00 62.73	6
50	ATOM	6201	Ö		D 162	44.490	74.439	40.425	1.00 60.67	8
	ATOM	6202	N		D 163	45.435	75.400	38.620		7
	ATOM	6203	CA	GLU :	D 163	44.149	75.861	38.139	1.00 66.60	6
	MOTA	6204	CB		D 163	44.325	76.984	37.105	1.00 69.72 1.00 72.12	6
55	ATOM	6205	CG		D 163	44.576	76.546 77.720	35.681 34.698	1.00 72.12	6 6
	MOTA ATOM	6206 6207	CD OF1	GLU . GLU .	D 163	44.506 45.442	78.557	34.703	1.00 75.59	8
	MOTA MOTA	6207	OE1		D 163	43.510	77.808	33.932	1.00 73.89	8
	MOTA	6209	C		D 163	43.310	74.712	37.572	1.00 65.25	6
60	MOTA	6210	ō		D 163	42.126	74.885	37.264	1.00 65.73	8
	MOTA	6211	N	TYR	D 164	43.926	73.539	37.448	1.00 64.10	7

•	WO 01/589	951			4		PCT/EP01/01457			
	ATOM	6212	CA	TYR D 164	-174 43.236	72.353	36.946	1.00 61.14	6	
	ATOM	6213	CB	TYR D 164		71.828	35.675	1.00 62.34	6	
	MOTA	6214	CG	TYR D 164		72.756	34.501	1.00 62.07	6	
	ATOM	6215		TYR D 164		73.264	33.887	1.00 62.29	6	
5	MOTA	6216		TYR D 164		74.152	32.813	1.00 64.14	6	
•	ATOM	6217		TYR D 164		73.151	34.016	1.00 63.36	6	
	ATOM	6218	CE2	TYR D 164		74.038	32.940	1.00 65.18	6	
	ATOM	6219	CZ	TYR D 164		74.536	32.337	1.00 65.18	6	
	ATOM	6220	ОН	TYR D 164		75.380	31.240	1.00 65.32	8	
10	ATOM	6221	C	TYR D 164		71.263	38.000	1.00 59.77	6	
	ATOM	6222	ō	TYR D 164		70.231	37.853	1.00 59.16	8	
	ATOM	6223	N	PHE D 165	44.008	71.497	39.068	1.00 57.70	7	
	ATOM	6224	CA	PHE D 165		70.518	40.143	1.00 56.00	6	
	MOTA	6225	СВ	PHE D 165	45.105	70.988	41.202	1.00 53.27	6	
15	MOTA	6226	CG	PHE D 165	45.635	69.885	42.053	1.00 51.93	6	
	MOTA	6227	CD1	PHE D 165	46.436	68.891	41.502	1.00 50.62	6	
	MOTA	6228		PHE D 165		69.820	43.398	1.00 52.41	6	
	MOTA	6229	CE1	PHE D 165		67.845	42.283	1.00 49.13	6	
	MOTA	6230	CE2	PHE D 165		68.777	44.188	1.00 52.20	6	
20	MOTA	6231	CZ	PHE D 165	46.608	67.788	43.624	1.00 51.98	6	
	MOTA	6232	С	PHE D 165		70.241	40.801	1.00 55.90	6	
	MOTA	6233	0	PHE D 165		71.149	41.005	1.00 56.82	8	
	MOTA	6234	N	SER D 166		68.980	41.126	1.00 55.56	7	
~-	MOTA	6235	CA	SER D 166		68.627	41.771	1.00 55.90	6	
25	MOTA	6236	CB	SER D 166		67.117	41.887	1.00 55.69	6	
	MOTA	6237	OG	SER D 166		66.799	42.457	1.00 55.69	8	
	ATOM	6238	C	SER D 166		69.229	43.158	1.00 56.73 1.00 56.74	б 8	
	ATOM	6239	0	SER D 160		69.229	43.839	1.00 57.58	7	
00	ATOM	6240	N	GLN D 16		69.729	43.578 44.892	1.00 57.81	6	
30	MOTA	6241	CA	GLN D 16'		70.353 71.383	44.892	1.00 57.81	6	
	ATOM	6242	CB	GLN D 16'		70.794	44.439	1.00 63.59	6	
	MOTA	6243	CG	GLN D 16'		71.854	44.107	1.00 65.57	6	
	MOTA	6244 6245	CD OF1	GEN D 16		72.607	44.979	1.00 65.98	8	
35	MOTA MOTA	6245		GLN D 16		71.909	42.831	1.00 65.54	7	
00	ATOM	6247	C	GLN D 16		69.328	45.977	1.00 56.65	6	
	ATOM	6248	Ö	GLN D 16		69.598	47.151	1.00 56.95	8	
	ATOM	6249	N	TYR D 16		68.145	45.586	1.00 56.16	7	
	ATOM	6250	CA	TYR D 16		67.091	46.556	1.00 53.65	6	
40	ATOM	6251	СВ	TYR D 16		66.297	46.096	1.00 54.14	6	
• • •	MOTA	6252	CG	TYR D 16	8 36.675	67.217	45.707	1.00 53.82	6	
	MOTA	6253	CD1	TYR D 16	8 36.446	67.545	44.371	1.00 53.19	6	
	MOTA	6254		TYR D 16		68.454	44.020	1.00 54.20	6	
	MOTA	6255		TYR D 16				1.00 52.39	6.	
45	MOTA	6256	CE2	TYR D 16		68.722	46.342	1.00 52.03	6	
	ATOM	6257	CZ	TYR D 16		69.035	45.016	1.00 53.04	6	
	MOTA	6258	ОН	TYR D 16		69.917	44.689	1.00 53.97	8	
	MOTA	6259	С	TYR D 16		66.162	46.851	1.00 52.39 1.00 53.02	6 8	
50	ATOM	6260	0	TYR D 16		65.185	47.575 46.299	1.00 53.02	7	
50	MOTA	6261	N	SER D 16		66.479	46.299	1.00 51.48	6	
	MOTA	6262	CA	SER D 16		65.686	45.584	1.00 52.14	6	
	ATOM	6263	CB	SER D 16		66.151 65.483	45.881	1.00 50.95	8	
	MOTA	6264	OG	SER D 16 SER D 16		65.828	47.953	1.00 53.72	6	
55	MOTA	6265	C	SER D 16		66.880	48.570	1.00 51.67	8	
55	ATOM	6266 6267	O N	ARG D 17		64.761	48.487	1.00 54.84	7	
	ATOM ATOM	6268	N CA	ARG D 17		64.778	49.850	1.00 54.97	6	
	ATOM	6269	CB	ARG D 17		63.366	50.297	1.00 54.29	6	
	ATOM	6270	CG	ARG D 17		62.647	51.081	1.00 57.60	6	
60	ATOM	6271	CD	ARG D 17		61.124	50.955	1.00 58.91	6	
50	MOTA	6272	NE	ARG D 17		60.543	51.323	1.00 61.45	7	
		· -								

-175 ATOM 6273 CZ ARG D 170 45.504 59.853 50.483 1.00	
AMOM 6273 CZ ARC D 170 45 504 59 853 50 483 1 00 5	CA 00 C
ATOM 6274 NH1 ARG D 170 45.140 59.656 49.220 1.00 ATOM 6275 NH2 ARG D 170 46.649 59.334 50.906 1.00	_
ATOM 6276 C ARG D 170 45.293 65.683 49.928 1.00	56.57 6
5 ATOM 6277 O ARG D 170 45.719 66.078 51.022 1.00	59.46 8
ATOM 6278 N PHE D 171 45.842 66.033 48.770 1.00	55.26 7
AION 02/3 CA 11111 2 11 11 11 11 11 11 11 11 11 11 1	54.09 6 53.61 6
MICH 0200 CD 2111 D 210 CA 600 AO FOR 4 00	53.61 6 54.38 6
ATOM 0201 CG 1111 D 171	55.63 6
	54.14 6
ATOM 6284 CE1 PHE D 171 47.521 62.415 48.694 1.00	54.27 6
ATOM 6285 CE2 PHE D 171 49.414 63.078 50.008 1.00	54.92 6
AIOM 0200 CZ IMB B 1/1	54.58 6
10 ATOM 0207 C TM2 5 111	53.25 6 52.23 8
ATOM 0200 0 1112 1 170 170 170 170 170 170 170 170 170 1	52.75 7
ATOM 0209 N 000 D 175	55.31 6
	58.80 6
20 ATOM 6292 CG GIJI D 172 48.293 71.616 49.686 1.00	62.32 6
ATOM 6293 CD GLU D 172 47.773 72.633 50.693 1.00	64.33 6
ATOM 0294 OEI GHO D 172	64.06 8 65.29 8
ATOM 0255 0H2 020 2 170	65.29 8 56.32 6
Alon 0290 C GD0 D 112	54.59 8
25 ATOM 0237 0 CHO D 173	56.82 7
	57.96 6
ATOM 6300 CB ILE D 173 50.062 72.033 43.644 1.00	57.06 6
ATOM 6301 CG2 ILE D 173 51.332 72.535 42.959 1.00	56.84 6
30 ATOM 6302 CG1 1BB 2 1/3	55.34 6 53.59 6
ATOM 0303 CDI 1111 D 173	59.20 6
ATOM 0304 C 1111 D 173	58.03 8
ATOM 6303 0 THE DITA 50.140 73.251 45.949 1.00	60.22 7
35 ATOM 6307 CA LEU D 174 52.784 74.473 46.394 1.00	61.88 6
ATOM 6308 CB LEU D 174 53.929 74.136 47.340 1.00	61.02 6
ATOM 6309 CG LEU D 174 53.512 73.196 48.469 1.00	61.46 6
ATOM 0310 CD1 DD0 D 1/4 01/1-	62.06 6 59.37 6
ATOM 6311 CD2 LEG D 174 52.303 75 103 45 151 1 00	63.17 6
40 ATOM 6512 C 1150 5 174 50 070 76 357 44 899 1 00	63.68 8
NOM 6314 N ASP D 175 54.080 74.479 44.349 1.00	64.58 7
ATOM 6315 CA ASP D 175 54.627 75.067 43.145 1.00	65.97 6
ATOM 6316 CB ASP D 175 55.789 75.993 43.538 1.00	67.34 6
45 ATOM 6317 CG ASP D 175 56.390 76.748 42.354 1.00	69.43 6 69.68 8
ATOM 0318 ODI ASI D 175	69.28 8
ATOM 6319 ODZ ASF D 173 57.005 73.004 42 164 1 00	66.38 6
ATOM 0320 C AST 5 175 55 300 73 846 42 561 1 00	66.58 8
	65.75 7
ATOM 6323 CA VAL D 176 55.536 73.436 39.831 1.00	65.19 6
ATOM 6324 CB VAL D 176 54.330 72.945 38.992 1.00	64.89 6
ATOM 6325 CGI VAL D 170	64.67 6 65.95 6
ATOM 6326 CG2 VAL B 176	66.36
JJ ATOM 0327 C VIII 2 176 56 170 75 214 39 513 1 00	66.32 8
ATOM 6329 N THE D 177 57.614 73.576 38.602 1.00	68.04 7
ATOM 6330 CA THR D 177 58.598 74.184 37.708 1.00	69.05
ATOM 6331 CB THR D 177 59.763 74.819 38.496 1.00	67.62 6
60 ATOM 6332 OG1 THR D 177 60.349 73.843 39.370 1.00	0 63.42 8
ATOM 6333 CG2 THR D 177 59.258 76.013 39.305 1.00	0 66.11 6

,	W O 01/36:	731						1 € 1/21 01/0140	, ,
					-176				
	MOTA	6334	С	THR D 177	59.165	73.144	36.739	1.00 71.66	6
	ATOM	6335	0	THR D 177	59.373	71.973	37.111	1.00 73.56	8
	ATOM	6336	N	GLN D 178	59.417	73.568	35.501	1.00 71.95	7
		6337		GLN D 178	59.941	72.667	34.488	1.00 72.06	6
5	MOTA		CA	GLN D 178	58.932	72.511	33.347	1.00 74.14	6
5	ATOM	6338	CB		57.466	72.700	33.754	1.00 76.97	6
	MOTA	6339	CG	GLN D 178		72.700	32.772	1.00 78.22	6
	MOTA	6340	CD	GLN D 178	56.497			1.00 78.22	8
	ATOM	6341		GLN D 178	56.603	72.230	31.551	1.00 75.44	7
	MOTA	6342		GLN D 178	55.544	71.266	33.302		6
10	MOTA	6343	С	GLN D 178	61.219	73.240	33.936	1.00 71.25	
	MOTA	6344	0	GLN D 178	61.226	74.368	33.462	1.00 71.24	8
	MOTA	6345	N	LYS D 179	62.291	72.461	33.979	1.00 71.70	7
	MOTA	6346	CA	LYS D 179	63.593	72.904	33.474	1.00 71.59	6
	ATOM	6347	CB	LYS D 179	64.553	73.170	34.642	1.00 73.63	6
15	MOTA	6348	CG	LYS D 179	63.906	73.953	35.800	1.00 77.80	6
	ATOM	6349	CD	LYS D 179	64.795	74.018	37.040	1.00 78.53	6
	MOTA	6350	CE	LYS D 179	64.016	74.470	38.273	1.00 79.16	6
	ATOM	6351	NZ	LYS D 179	62.899	73.537	38.610	1.00 77.90	7
	ATOM	6352	C	LYS D 179	64.173	71.807	32.601	1.00 70.50	6
20	ATOM	6353	0	LYS D 179	64.549	70.754	33.112	1.00 69.32	8
20		6354		LYS D 180	64.252	72,044	31.294	1.00 69.56	7
	ATOM		N	LYS D 180	64.803	71.039	30.382	1.00 69.55	6
	MOTA	6355	CA		64.581	71.464	28.924	1.00 69.05	6
	MOTA	6356	CB	LYS D 180	65.462	72.584	28.419	1.00 68.35	6
05	MOTA	6357	CG	LYS D 180		72.041	27.860	1.00 66.86	6
25	MOTA	6358	CD	LYS D 180	66.773		26.619	1.00 63.97	6
	MOTA	6359	CE	LYS D 180	66.550	71.200		1.00 64.54	7
	MOTA	6360	NZ	LYS D 180	66.096	72.020	25.476	1.00 68.87	6
	ATOM	6361	С	LYS D 180	66.293	70.795	30.642		
	MOTA	6362	0	LYS D 180	66.869	71.406	31.536	1.00 69.83	8
30	ATOM	6363	N	ASN D 181	66.905	69.879	29.897	1.00 68.37	7
	MOTA	6364	CA	ASN D 181	68.326	69.615	30.060	1.00 70.05	6
	ATOM	6365	CB	ASN D 181	68.711	69.461	31.540	1.00 70.86	6
	ATOM	6366	CG	ASN D 181	67.808	68.533	32.291	1.00 71.68	6
	ATOM	6367	OD1	ASN D 181	67.498	67.446	31.823	1.00 74.38	8
35	ATOM	6368		ASN D 181	67.395	68.945	33.487	1.00 72.61	7
-	ATOM	6369	C	ASN D 181	68.905	68.449	29.281	1.00 70.12	6
	ATOM	6370	ō	ASN D 181	68.535	67.303	29.491	1.00 68.91	8
	ATOM	6371	N	SER D 182	69.844	68.760	28.385	1.00 71.81	7
	ATOM	6372	CA	SER D 182	70.519	67.744	27.577	1.00 71.83	6
40			CB	SER D 182	71.361	68.418	26.495	1.00 70.60	6
40	ATOM	6373		SER D 182	71.817	67.463	25.557	1.00 71.86	8
	MOTA	6374	OG		71.405	66.866	28.482	1.00 71.03	6
	MOTA	6375	C	SER D 182	71.794	67.281	29.572	1.00 72.13	8
	MOTA	6376		SER D 182	71.715	65.653	28.037	1.00 70.45	7
	MOTA	6377		VAL D 183			28.842	1.00 69.61	6
45	ATOM	6378		VAL D 183	72.528		30.066	1.00 69.93	6
	MOTA	6379	СВ	VAL D 183	71.728	64.221		1.00 71.71	6
	MOTA	6380		L VAL D 183	70.268	63.988	29.671	1.00 68.31	6
	MOTA	6381	CG2	2 VAL D 183	72.331	62.909	30.584		
	MOTA	6382	C	VAL D 183	73.046	63.521	28.069	1.00 69.82	6
50	ATOM	6383	0	VAL D 183	72.317		27.305	1.00 69.28	8
	MOTA	6384		THR D 184	74.314	63.194	28.272	1.00 71.03	7
	ATOM	6385		THR D 184	74.898	62.041	27.596	1.00 72.40	6
	ATOM	6386			.76.314	62.360	27.027	1.00 71.67	6
	MOTA	6387		1 THR D 184	76.207		26.010	1.00 69.65	8
55					76.944		26.404	1.00 71.24	6
33	MOTA	6388		THR D 184	74.997		28.602		6
	MOTA	6389		THR D 184	75.273		29.786		8
	MOTA	6390		TYR D 184	74.749		28.139		7
	MOTA	6391			74.818		29.024		6
00	ATOM	6392			73.477		-		6
60	MOTA	6393			72.286			_	6
	MOTA	6394	4 CG	TYR D 185	12.200	. 50.057	25,524		_

	W O 01/36	731						101/2101/01	•
					-177				
	N COM	6395	CD1	TYR D 185	71.822	59.527	28.362	1.00 77.16	6
	ATOM			TYR D 185	70.781			1.00 78.65	6
	ATOM	6396			71.676	58.643		1.00 78.44	6
	ATOM	6397		TYR D 185	70.629	59.532		1.00 78.76	6
_	MOTA	6398		TYR D 185				1.00 78.44	6
5	MOTA	6399		TYR D 185	70.190	60.417			8
	ATOM	6400		TYR D 185	69.173	61.311	30.160	1.00 78.64	
	ATOM	6401		TYR D 185	75.909	57.595		1.00 76.37	6
	MOTA	6402	0	TYR D 185	76.062	57.403	27.320	1.00 75.86	8
	MOTA	6403	N	SER D 186	76.669	57.031	29.454	1.00 78.41	7
10	ATOM	6404		SER D 186	77.762	56.127	29.097	1.00 80.47	6
. •	ATOM	6405	CB	SER D 186	78.353	55.494	30.361	1.00 80.37	6
	ATOM	6406	OG	SER D 186	77.324	55.000	31.202	1.00 80.82	8
	ATOM	6407	C	SER D 186	. 77.259	55.042	28.139	1.00 81.49	6
	ATOM	6408	Ö	SER D 186	77.977	54.637	27.205	1.00 80.86	8
15	ATOM	6409	N	CYS D 187	76.018	54.601	28.370	1.00 82.03	7
13		6410	CA	CYS D 187	75.366	53.573	27.553	1.00 82.11	6
	ATOM			CYS D 187	75.259	54.005	26.123	1.00 82.74	6
	ATOM	6411	C	CYS D 187	75.445	53.226	25.179	1.00 81.67	8
	MOTA	6412	0	CYS D 187	73.908	53.360	27.980	1.00 82.28	6
00	ATOM	6413	CB	CYS D 187	72.725	54.778	27.707	1.00 81.64	16
20	MOTA	6414	SG		74.954	55.287	25.990	1.00 83.43	7
	MOTA	6415	N	CYS D 188		55.827	24.701	1.00 83.03	6
	MOTA	6416	CA	CYS D 188	74.614	57.070	24.204	1.00 81.94	6
	MOTA	6417	С	CYS D 188	75.379		24.860	1.00 81.77	8
	MOTA	6418	0	CYS D 188	75.401	58.127	24.777	1.00 83.56	6
25	MOTA	6419	CB	CYS D 188	73.091	56.059	25.740	1.00 85.15	16
	MOTA	6420	SG	CYS D 188	72.115	54.783		1.00 80.60	7
	MOTA	6421	N	PRO D 189	76.000	56.945	23.013	1.00 80.05	6
	MOTA	6422	CD	PRO D 189	75.862	55.676	22.263	1.00 78.99	6
	MOTA	6423	CA	PRO D 189	76.809	57.921	22.254	1.00 78.33	6
30	ATOM	6424	CB	PRO D 189	76.804	57.341	20.836		6
	ATOM	6425	CG	PRO D 189	76.835	55.852	21.097	1.00 80.06	
	ATOM	6426	С	PRO D 189	76.386	59.408	22.258	1.00 76.71	6 8
	ATOM	6427	0	PRO D 189	77.106	60.265	22.777	1.00 76.06	
	MOTA	6428	N	GLU D 190	75.237	59.713	21.663	1.00 73.54	7
35	MOTA	6429	CA	GLU D 190	74.762	61.101	21.583	1.00 70.67	6
-	ATOM	6430	CB	GLU D 190	73.735	61.233	20.462	1.00 72.95	6
	ATOM	6431	CG	GLU D 190	73.941	60.272	19.292	1.00 76.22	6
	MOTA	6432		GLU D 190	74.959	60.778	18.284	1.00 77.17	6
	ATOM	6433			74.920	61.987	17.949	1.00 75.78	8
40	MOTA	6434			75.786	59.961	17.819	1.00 78.06	8
40		6435		GLU D 190	74.113	61.576	22.874	1.00 67.13	6
	MOTA	6436		GLU D 190	74.060	60.842	23.861	1.00 66.77	8
	MOTA	6437		ALA D 191	73.595	62.797	22.852	1.00 63.73	7
	MOTA	6438		ALA D 191	72.924	63.362	24.027	1.00 63.96	6
	ATOM			ALA D 191	73.293	64.833	24.188	1.00 60.91	6
45	ATOM	6439		ALA D 191	71.398		23.935	1.00 63.09	6
	MOTA	6440		ALA D 191	70.824		22.848	1.00 63.27	8
	ATOM	6441		TYR D 192	70.737		25.073	1.00 61.86	7
	MOTA	6442			69.284		25.077	1.00 60.02	6
	ATOM	6443		TYR D 192	68.874		25.544	1.00 58.87	6
50		6444		TYR D 192	69.185		24.531	1.00 59.77	6
	MOTA	6445		TYR D 192	70.447				6
	MOTA	6446	CD:	1 TYR D 192			23.514		6
	ATOM	644		1 TYR D 192	70.762		23.568		6
	MOTA	644		2 TYR D 192	68.234				6
55	MOTA	644			68.534	59.084			6
	ATOM	645	0 CZ	TYR D 192	69.803				8
	ATOM	645	1 OH		70.120				6
	ATOM	645	2 C	TYR D 192	68.590				8
	MOTA		3 0	TYR D 192	68.594				
60	MOTA (645	4 N	GLU D 193	67.986				
	MOTA	645	5 CA	GLU D 193	67.280	65.992	25.915	, 1.00 00.40	J

PCT/EP01/01457

						-1/0				
	ATOM	6456	CB G	LU D	193	66.832	67.054	24.898	1.00 61.02	6
	MOTA	6457		FLU D		67.985	67.781	24.196	1.00 65.53	6
	MOTA	6458		TU D		67.522	68.937	23.292	1.00 66.58	6
	MOTA	6459		ELU D		66.678	69.760	23.739	1.00 66.15	8
5	MOTA	6460		GLU D		68.017	69.023	22.138	1.00 66.88	8
	ATOM	6461		GLU D		66.066	65.455	26.658	1.00 61.32	6
	MOTA	6462		GLU D		65.498	64.428	26.278	1.00 61.10	8
	ATOM	6463		ASP D		65.682	66.157	27.724	1.00 62.11	7 6
	MOTA	6464		ASP D		64.533	65.788	28.537	1.00 60.32	6
10	MOTA	6465		ASP D		64.855	64.571	29.416	1.00 60.68	6
	MOTA	6466		ASP D		65.759	64.907	30.589	1.00 61.25 1.00 62.58	8
	MOTA	6467	OD1	ASP D	194	66.929	64.453	30.591		8
	MOTA	6468		ASP D		65.297	65.619	31.509	1.00 61.10 1.00 59.85	6
	MOTA	6469		ASP D		64.086	66.951	29.417	1.00 59.83	8
15	MOTA	6470		ASP D		64.890	67.793	29.816	1.00 57.38	7
	MOTA	6471		VAL D		62.792	66.993	29.704	1.00 57.36	6
	ATOM	6472		VAL D		62.225	68.024	30.538 30.001	1.00 52.24	6
	MOTA	6473		VAL D		60.864	68.480	31.001	1.00 52.24	6
	ATOM	6474		VAL D		60.179	69.394	28.693	1.00 52.14	6
20	MOTA	6475		VAL D		61.058	69.189	31.935	1.00 56.36	6
	MOTA	6476		VAL D		62.044	67.460 66.412	32.114	1.00 57.76	8
	MOTA	6477	-	VAL D		61.452	68.151	32.114	1.00 58.67	7
	MOTA	6478	N	GLU D		62.571 62.425	67.712	34.303	1.00 58.26	6
~=	MOTA	6479		GLU D		63.754	67.833	35.035	1.00 58.61	6
25	ATOM	6480		GLU D		63.725	67.326	36.460	1.00 61.95	6
	ATOM	6481	CG	GLU I		65.062	67.533	37.172	1.00 63.50	6
	ATOM	6482	CD OF1	GLU I		66.083	67.014	36.679	1.00 62.21	8
	ATOM	6483	OEI	GLU I	196	65.099	68,218	38.222	1.00 65.74	8
30	ATOM	6484 6485	C	GLU I		61.370	68.598	34.959	1.00 58.08	6
30	MOTA	6486	0	GLU I		61.500	69.822	34.997	1.00 59.87	8
	MOTA	6487	N	VAL I		60.305	67.979	35.452	1.00 57.22	7
	ATOM ATOM	6488	CA	VAL I		59.242	68.721	36.104	1.00 54.36	6
	ATOM	6489	CB	VAL I		57.863	68.304	35.567	1.00 52.68	6
35	ATOM	6490		VAL I		56.772	69.095	36.255	1.00 49.60	6
00	ATOM	6491		VAL I		57.809	68.517	34.068	1.00 50.84	6
	ATOM	6492	Ċ		197	59.317	68.420	37.587	1.00 55.10	6
	ATOM	6493	Ō	VAL I	D 197	59.367	67.264	37.995	1.00 55.27	8
	АТОМ	6494	N		D 198	59.351		38.399	1.00 56.68	7 6
40	ATOM	6495	CA		D 198	59.413	69.284	39.839	1.00 56.39 1.00 55.89	6
	MOTA	6496	CB		D 198	60.487		40.448	1.00 57.83	8
	ATOM	6497	OG		D 198	61.789		40.066	1.00 56.61	6
	ATOM	6498	С		D 198	58.058		40.448	1.00 56.25	8
	MOTA	6499	0		D 198	57.536		40.317 41.101	1.00 56.92	7
45	MOTA	6500			D 199	57.481		41.728		6
	MOTA	6501			D 199	56.189			1.00 57.08	6
	MOTA	6502			D 199	55.303		41.468	1.00 57.99	6
	MOTA	6503	CG		D 199	53.981 53.094				6
	ATOM	6504		LEU	D 199	53.094				6
50	MOTA	6505		LEU	D 199	56.354		43.220		6
	MOTA	6506			D 199	56.625				8
	MOTA	6507		DEU	D 199 D 200	-56.207				7
	ATOM	6508			D 200	56.315				6
EE	MOTA	6509			D 200	57.017			1.00 59.47	6
55	MOTA			MDV	D 200	57.12				6
	MOTA				D 200	57.50			1.00 60.78	8
	ATOM ATOM			NZA S	D 200	56.79			1.00 63.13	
	MOTA			ASN	D 200	54.88		45.593	1.00 55.28	6
60				ASN	D 200	54.10	8 71.422			
	ATOM			PHE	D 201	54.54	9 69.554	46.419	1.00 53.26	7

PCT/EP01/01457

WO 01/58951

						-179				
	ATOM	6517	CA	PHE D 2	201	53.218	69.444	46.973	1.00 51.91	6
	ATOM	6518	CB	PHE D 2		52.408	68.434	46.168	1.00 49.89	6
	MOTA	6519	CG	PHE D 2	201	52.870	67.013	46.348	1.00 46.59	6
	MOTA	6520		PHE D 2		52.068	66.086	47.003	1.00 45.61	6 6
5	MOTA	6521		PHE D 2		54.133	66.613	45.903 47.218	1.00 46.86 1.00 45.68	. 6
	MOTA	6522		PHE D		52.519 54.597	64.779 65.312	46.112	1.00 44.48	6
	MOTA	6523		PHE D 2		53.788	64.394	46.772	1.00 44.43	6
	ATOM ATOM	6524 6525	CZ C	PHE D		53.360	68.940	48.386	1.00 53.35	6
10	MOTA	6526	0	PHE D		54.456	68.570	48.818	1.00 52.18	8
. •	ATOM	6527	N	ARG D		52.238	68.902	49.093	1.00 55.22	7
	MOTA	6528	CA	ARG D	202	52.211	68.426	50.470	1.00 57.74	6
	ATOM	6529	CB	ARG D		52.632	69.546	51.412	1.00 58.53	6
	MOTA	6530	CG	ARG D		51.564	70.612	51.484	1.00 62.76 1.00 64.76	6 6
15	MOTA	6531	CD	ARG D		51.956	71.797	52.313 52.296	1.00 64.76	7
	MOTA	6532	NE	ARG D		50.901 51.046	72.806 74.035	52.779	1.00 65.00	6
	MOTA	6533	CZ	ARG D ARG D		52.206	74.409	53.323	1.00 65.86	7
	ATOM ATOM	6534 6535	NH2			50.045	74.896	52.708	1.00 62.46	7
20	MOTA	6536	C	ARG D		50.788	67.997	50.835	1.00 57.64	6
	ATOM	6537	Ö	ARG D		49.822	68.392	50.186	1.00 55.63	8
	MOTA	6538	N	LYS D		50.668	67.189	51.878	1.00 58.55	7
	MOTA	6539	CA	LYS D		49.359	66.759	52.332	1.00 59.55 1.00 60.97	6 6
	MOTA	6540	CB	LYS D		49:505	65.708	53.428 54.031	1.00 60.97	6
25	MOTA	6541	CG		203	48.195	65.258 64.319	55.194	1.00 66.11	6
	MOTA	6542	CD	LYS D		48.445 47.142	63.813	55.784	1.00 68.33	6
	MOTA	6543 6544	CE NZ	LYS D	203	46.380	62.985	54.804	1.00 69.98	7
	MOTA MOTA	6545	C	LYS D		48.702	68.008	52.914	1.00 60.27	6
30	MOTA	6546	ō		203	49.402	68.886	53.428	1.00 60.55	8
-	ATOM	6547	N	LYS D		47.374	68.105	52.832	1.00 59.32	7
	ATOM	6548	CA	LYS D		46.680	69.260	53.395	1.00 60.40 1.00 59.66	6 6
	MOTA	6549	CB	LYS D		45.221	69.284	52.947 51.495	1.00 56.15	6
	MOTA	6550	CG	LYS D		45.054	69.738 69.489	50.974	1.00 52.10	6
35	ATOM	6551	CD	LYS D LYS D	204	43.652 43.593	69.775	49.488	1.00 52.88	6
	MOTA	6552 6553	CE NZ	LYS D		42.334	69.320	48.856	1.00 54.65	7
	MOTA MOTA	6554	C	LYS D		46.776	69.201	54.919	1.00 62.27	6
	MOTA	6555	o	LYS D		47.031	68.129	55.479	1.00 63.85	8
40	MOTA	6556	N	GLY D		46.590	70.344	55.587	1.00 61.70	7
	MOTA	6557	CA	GLY D		46.701	70.390	57.043	1.00 61.46 1.00 60.96	6 6
	MOTA	6558		GTA D		45.432	70.704	57.821	1.00 60.96	8
	MOTA	6559		1 GLY D		44.364	70.809 70.835	57.191 59.067	1.00 60.53	
45	MOTA	6560		2 GLY D	205	45.495 68.481	57.493	1.362	1.00 63.85	
45	MOTA	6561		PHE E	1	68.496	56.384	0.357	1.00 65.93	
	MOTA MOTA	6562 6563		1 PHE E	1	67.431	56.207	-0.526	1.00 67.13	6
	MOTA	6564		2 PHE E	1	69.549	55.462	0.345	1.00 67.48	6
	MOTA	6565		1 PHE E		67.410		-1.409	1.00 68.65	6
50	MOTA	6566		2 PHE E		69.548				6
	MOTA	6567	CZ			68.481		-1.406		
	MOTA	6568		PHE E		67.191		2.218 3.225		
	MOTA	6569		PHE E		67.898 68.457				
	MOTA	6570		PHE E		67.655				
55	MOTA MOTA	6571 6572		ASP E		66.011			1.00 61.01	. 7
	MOTA	6573				65.524			1.00 60.82	
	MOTA	6574				64.448	61.754			
	ATOM	6575	5 CG	ASP E	2	63.263				
60		657	6 OI	1 ASP E		62.587				
	ATOM	657	7 OI	2 ASP E	2	63.006	61.396	1.142	, 1.00 00.90	, 0

PCT/EP01/01457

WO 01/58951

							-180				_
	MOTA	6578	С	ASP E	2		65.012	59.731		1.00 60.89	6
	MOTA	6579	0	ASP E	2		64.990	58.525	4.216	1.00 62.95	8
	MOTA	6580	N	ARG E	3		64.624	60.214	5.635	1.00 60.20	7
	MOTA	6581	CA	ARG E	3		64.161	59.321	6.697	1.00 57.08	6
5	MOTA	6582	CB	ARG E	3		63.746	60.128	7.933	1.00 56.21	6
	MOTA	6583	CG	ARG E	3		64. 906.	60.475	8.878	1.00 56 67	6
	MOTA	6584	CD	ARG E	3		65.314	59.266	9.702	1.00 57.53	6
	MOTA	6585	NE	ARG E	3		66.519	59.426	10.524	1.00 58.61	7
	ATOM	6586	CZ	ARG E	3		66.825	60.497	11.258	1.00 60.79	6
10	ATOM	6587	NH1	ARG E	3		66.024	61.559	11.294	1.00 61.35	7
	MOTA	6588	NH2	ARG E	3		67.943	60.499	11.975	1.00 58.97	7
	ATOM	6589	С	ARG E	3		63.008	58.447	6.244	1.00 56.93	6
	ATOM	6590	0	ARG E	3		62.949	57.256	6.567	1.00 58.08	8
	ATOM	6591	N	ALA E	4		62.102	59.033	5.473	1.00 54.21	7
15	MOTA	6592	CA	ALA E	4		60.937	58.311	4.993	1.00 52.85	6
	ATOM	6593	CB	ALA E	4		60.002	59.262	4.270	1.00 50.53	6
	MOTA	6594	С	ALA E	4		61.342	57.168	4.075	1.00 53.00	6
	MOTA	6595	0	ALA E	4		60.858	56.056	4.225	1.00 53.30	8
	MOTA	6596	N	ASP E	5		62.235	57.443	3.132	1.00 54.00	7
20	MOTA	6597	CA	ASP E	5		62.692	56.433	2.190	1.00 54.02	6
	ATOM	6598	СВ	ASP E	5		63.702	57.021	1.197	1.00 56.37	6
	ATOM	6599	CG	ASP E	5		63.153	58.223	0.435	1.00 60.25	6
	MOTA	6600	OD1	ASP E	5		62.018	58.154	-0.072	1.00 61.70	8
	ATOM	6601	OD2	ASP E	5		63.864	59.247	0.327	1.00 64.63	8
25	ATOM	6602	С	ASP E	5		63.341	55.278	2.924	1.00 54.45	6
	ATOM	6603	0	ASP E	5		63.192	54.127	2.532	1.00 54.26	8
	MOTA	6604	N	ILE E	6		64.060	55.582	3.997	1.00 54.54	7
	MOTA	6605	CA	ILE E	6		64.734	54.535	4.755	1.00 55.28	6
	MOTA	6606	CB	ILE E	6		65.727	55.121	5.781	1.00 56.90	6
30	MOTA	6607	CG2	ILE E	6		66.476	53.991	6.489	1.00 56.40	6 6
	ATOM	6608	CG1	ILE E	6		66.728	56.031	5.068	1.00 58.74	6
	MOTA	6609	CD1	ILE E	6		67.833	56.589	5.976	1.00 60.73	6
	MOTA	6610	С	ILE E	6		63.765	53.617	5.482	1.00 53.47	8
	MOTA	6611	0	ILE E	6		63.830	52.401	5.322	1.00 53.23	7
35	ATOM	6612	N	LEU E	7		62.883	54.199	6.290	1.00 53.23	6
	ATOM	6613	CA	LEU E	7		61.897	53.423	7.033	1.00 52.57	6
	MOTA	6614	CB	LEU E	7		61.060	54.354	7.899	1.00 52.03	6
	ATOM	6615		LEU E	7		61.862	55.020	9.017	1.00 52.39	6
	MOTA	6616	CD:	1 LEU E	7		61.074	56.183	9.607	1.00 53.72	6
40	MOTA	6617		2 LEU E	7		62.185	53.989	10.070	1.00 47.50	
	ATOM	6618		LEU E	7		61.003	52.660	6.065	1.00 52.40	6 8
	MOTA	6619	0	LEU E	7		60.665	51.503	6.302	1.00 53.43	7
	ATOM	6620		TYR E	8		60.644		4.967	1.00 51.20	6
	ATOM	6621	. CA	TYR E	8		59.810	52.707	3.951	1.00 52.74	6
45	ATOM	6622	CB	TYR E	8		59.622	53.686	2.804	1.00 54.75	
	ATOM	6623			8		58.825		1.660	1.00 60.00	6 6
	MOTA	6624		1 TYR E	8	-	57.448		1.773	1.00 59.81	
	ATOM	6625	CE	1 TYR E	8		56.723		0.734		6 6
	MOTA	6626		2 TYR E	8		59.453		0.465		
50	MOTA	6621			8		58.727		-0.580		6
	ATOM	6628		TYR E	8		57.367		-0.433		6
	ATOM	662			8		56.646		-1.457		8
	MOTA	663		TYR E	8		60.399				6
	MOTA	663		TYR E	8		59.692	50.414			8
55		663		ASN E	9		61.688				7
	MOTA	663			9		62.338				6
	ATOM	663		·	9		63.790				6
	ATOM			_	9		63.907			1.00 62.10	6
	MOTA			O1 ASN E	9		62.908				8
60				2 ASN E	9		65.137				7
	ATOM			ASN E			62.297	7 49.112	3.584	1 1.00 52.17	6
			_								

PCT/EP01/01457

						101				
					•	-181	40 003	3.287	1.00 51.04	8
	MOTA	6639	0	ASN E	9	61.870	48.003 49.410		1.00 53.05	7
	MOTA	6640	N	ILE E	10	62.746 62.752	48.424		1.00 53.91	6
	ATOM	6641	CA	ILE E	10	63.189	49.053		1.00 53.67	6
_	MOTA	6642	CB	ILE E	10	63.169	48.027	8.316	1.00 51.86	6
5	ATOM	6643	CG2		10	64.627	49.564	7.077	1.00 51.89	6
	MOTA	6644		ILE E	10	65.085	50.379	8.251	1.00 50.06	6
	MOTA	6645		ILE E	10	61.358	47.835	6.054	1.00 55.10	6
	MOTA	6646	C	ILE E	10 10	61.186	46.631	6.216	1.00 55.00	8
40	MOTA	6647	0	ILE E	11	60.364	48.708	6.032	1.00 56.28	7
10	MOTA	6648	N	ARG E	11	58.975	48.308	6.199	1.00 57.92	6
	MOTA	6649	CA	ARG E	11	58.084	49.543	6.106	1.00 61.96	6
	MOTA	6650	CB CG	ARG E	11	56.628	49.280	6.323	1.00 69.38	6
	MOTA	6651	CD	ARG E	11	56.359	49.040	7.797	1.00 79.46	6
15	MOTA	6652 6653	NE	ARG E	11	54.957	49.274	8.149	1.00 85.84	7
15	MOTA	6654	CZ	ARG E	11	54.244	50.315	7.713	1.00 89.11	6
	MOTA	6655		ARG E	11	54.801	51.215	6.892	1.00 90.35	7
	MOTA	6656		ARG E	11	52.980	50.475	8.117	1.00 90.14	7
	MOTA	6657	C	ARG E	11	58.559	47.314	5.126	1.00 56.77	6
20	ATOM ATOM	6658	o	ARG E	11	57.986	46.264	5.415	1.00 55.32	8
20	MOTA	6659	N	GLN E	12	58.866	47.663	3.881	1.00 56.51	7
	MOTA	6660	CA	GLN E	12	58.511	46.850	2.730	1.00 54.24	6
	ATOM	6661	CB	GLN E	12	58.583	47.698	1.485	1.00 53.75	6
	MOTA	6662	CG	GLN E	12	57.341	47.645	0.673	1.00 58.35	6
25	ATOM	6663	CD	GLN E	12	56.287	48.540	1.223	1.00 59.21	6
	ATOM	6664	OE1		12	56.517	49.726	1.375	1.00 63.59	8
	MOTA	6665	NE2		12	55.121	47.990	1.528	1.00 59.83	7
	ATOM	6666	C	GLN E	12	59.312	45.581	2.484	1.00 53.65	6
	MOTA	6667	0	GLN E	12	58.820	44.677	1.825	1.00 52.67	8 7
30	ATOM	6668	N	THR E	13	60.536	45.507	2.995	1.00 54.14	6
	MOTA	6669	CA	THR E	13	61.369	44.331	2.771	1.00 55.96 1.00 55.93	6
	MOTA	6670	CB	THR E	13	62.714	44.726	2.181	1.00 55.29	8
	MOTA	6671	OG:	THR E	13	63.380	45.612	3.090	1.00 55.33	6
	MOTA	6672	CG2			62.526	45.400	0.822	1.00 58.24	6
35	MOTA	6673	С	THR E		61.656	43.486	4.005 3.892	1.00 58.85	8
	MOTA	6674	0	THR E		62.096		5.182	1.00 60.49	7
	MOTA	6675	N	SER E		61.414		6.408	1.00 61.17	6
	MOTA	6676		SER E		61.681		7.599	1.00 62.69	6
	MOTA	6677		SER E		61.629 62.247		8.723	1.00 66.18	8
40	MOTA	6678		SER E		60.727		6.644	1.00 60.36	6
	ATOM	6679		SER E		59.579		6.184	1.00 59.94	8
	ATOM	6680		SER E		61.233		7.369	1.00 58.70	7
-	MOTA	6681		ARG E		60.487		7.703	1.00 58.01	6
4 =	ATOM	6682				60.926		6.805	1.00 57.94	6
45	ATOM	6683				60.686		5.325	1.00 59.93	6
	MOTA	6684 6685				60.746		4.547	1.00 63.77	6
	MOTA	6686		_		59.755		5.060	1.00 66.81	7
	MOTA MOTA	6687				59.714		4.772	1.00 66.79	6
50	MOTA	6688		1 ARG		60.622	34.982	3.964	1.00 64.79	7
50	MOTA	6689		2 ARG	E 15	58.748	34.752	5.287		7
	MOTA	6690		ARG		60.743	39.621	9.170		6
	ATOM	6693		ARG		61.709	38.928	9.513		8
	ATOM	6693		PRO		59.869		10.057		7
55		669				58.682		9.727		6
5 5	ATOM					59.96		11.503		6
	ATOM			_		58.73		12.031		6
	MOTA			PRO		58.46		10.997		6 6
	MOTA					59.98		11.945		8
60			8 0	PRO		60.41		13.046		7
	ATOM		9 N	ASP	E 17	59.51	2 37.579	11.095	, 1.00 30.70	•

PCT/EP01/01457

						1	82				
		6700	<i>a</i> 7	. CD E	17		. 477	36.171	11.446	1.00 53.11	6
	MOTA	6700 6701		ASP E ASP E	17		. 244	35.492	10.832	1.00 58.78	6
	MOTA MOTA	6702		ASP E	17		.931	35.917	11.513	1.00 64.95	6
	ATOM	6703		ASP E	17	56	. 959	36.261	12.732	1.00 65.29	8
5	ATOM	6704		ASP E	17	55	.865	35.887	10.831	1.00 66.80	8
_	ATOM	6705		ASP E	17		.716	35.401	11.039	1.00 52.04	6
	ATOM	6706	0 2	ASP E	17		.787	34.194	11.242	1.00 53.16	8 7
	MOTA	6707	N A	VAL E	18		.701	36.090	10.481	1.00 52.13 1.00 51.75	6
	MOTA	6708		VAL E	18		.906	35.410	10.034 8.509	1.00 51.75	6
10	MOTA	6709		VAL E	18		.050	35.519 34.728	8.037	1.00 54.22	6
	MOTA	6710		VAL E	18		.265 .797	35.010	7.843	1.00 52.93	6
	MOTA	6711		VAL E	18 18		.193	35.897	10.675	1.00 50.84	6
	MOTA	6712		VAL E VAL E	18		.595	37.039	10.513	1.00 50.74	8
4 5	MOTA	6713		ILE E	19		.841	34.990	11.387	1.00 51.04	7
15	MOTA	6714 6715		ILE E	19		.092	35.270	12.077	1.00 53.80	6
	MOTA	6716		ILE E	19		.478	34.027	12.940	1.00 52.99	6
	MOTA MOTA	6717		ILE E	19		.791	32.842	12.040	1.00 52.72	6
	ATOM	6718		ILE E	19	67	.644	34.346	13.870	1.00 52.81	6
20	ATOM	6719		ILE E	19		7.867	33.290	14.923	1.00 49.41	6 6
	ATOM	6720	С	ILE E	19		7.184	35.628	11.053	1.00 55.50 1.00 54.87	8
	ATOM	6721	0	ILE E	19		7.399	34,903	10.087	1.00 54.87	7
	MOTA	6722	N	PRO E	20		7.879	36.765	11.250	1.00 57.00	6
	MOTA	6723	CD	PRO E	20		7.710	37.684	12.385 10.359	1.00 60.68	6
25	MOTA	6724	CA	PRO E	20		3.948	37.253 38.664	10.897	1.00 58.99	6
	MOTA	6725	CB	PRO E	20		9.252 8.056	39.007	11.744	1.00 60.19	6
	ATOM	6726	CG	PRO E	20		0.201	36.370	10.360	1.00 62.73	6
	ATOM	6727	C	PRO E	20 20		1.317	36.854	10.568	1.00 61.22	8
20	MOTA	6728	N O	THR E	21		0.008	35.080	10.117	1.00 65.32	7
30	MOTA	6729 6730	CA	THR E	21		1.107	34.128	10.106	1.00 69.19	6
	MOTA MOTA	6731	CB	THR E		7	0.573	32.698	10.364	1.00 68.56	6
	MOTA	6732		THR E		7	0.744		11.751	1.00 66.59	8 6
	MOTA	6733		THR E			1.300		9.502	1.00 68.21 1.00 72.78	6
35	ATOM	6734	С	THR E			1.964		8.840	1.00 72.75	8
	MOTA	6735	0	THR E			1.450		7.716 9.051	1.00 77.19	7
	MOTA	6736		GLN E			3.282		7.971	1.00 80.45	6
	ATOM	6737		GLN E			4.279 5.303			1.00 81.20	6
	ATOM	6738		GLN E			4.691			1.00 83.07	б
40	MOTA	6739		GLN E			75.515			1.00 85.11	6
	MOTA	6740		GLN E			75.640			1.00.85.67	8
	MOTA	6741 6742					76.087		8.510		7
	MOTA	6743		GLN I			74.980	32.739			6
45	MOTA MOTA	6744		GI'N I		•	75.783				8
70	MOTA	6745		ARG I			74.676				7 6
	MOTA	6746		ARG I	E 23		75.23				6
	ATOM	6747		ARG 1			76.76				6
	MOTA	6748	3 CG	ARG :			77.31				6
50	MOTA	6749		ARG			77.78				
	MOTA			ARG			78.14 78.98				6
	MOTA						79.59			1.00 92.22	7
	MOTA			1 ARG 2 ARG			79.20			7 1.00 92.78	7
	MOTA			2 ARG ARG			74.79			7 1.00 85.32	
55			_	ARG			73.67			7 1.00 85.55	
	MOTA MOTA			ASP			75.64	8 28.84			
	ATOM						75.30		2 9.90	45	6
	MOTA						76.10				6
60			9 CG	ASP			76.67				
	MOTA			1 ASP	E 24		75.85	6 26.08	۷ / ۱ ، ۵۶		

	W O 01/30	9931								2027-2-0-0-0	
							-183				_
		cac1	000	ASP E	24		77.930	26.212		1.00 94.96	8
	MOTA	6761		ASP E	24		75.657	28.917	11.116	1.00 84.76	6
	MOTA	6762	C		24		75.551	28.466	12.259	1.00 84.92	8
	MOTA	6763	0	ASP E			76.097	30.146	10.857	1.00 82.51	7
_	MOTA	6764	N	ARG E	25		76.465	31.063	11.930	1.00 80.45	6
5	MOTA	6765	CA	ARG E	25			32.289	11.382	1.00 83.04	6
	MOTA	6766	CB	ARG E	25		77.208	32.032	10.918	1.00 87.73	6
	MOTA	6767	CG	ARG E	25		78.635		10.688	1.00 91.97	6
	MOTA	6768	CD	ARG E	25		79.370	33.358	10.340	1.00 95.94	7
	MOTA	6769	NE	ARG E	25		80.781	33.171		1.00 97.73	6
10	MOTA	6770	CZ	ARG E	25		81.667	34.164	10.199	1.00 98.12	7
. •	MOTA	6771	NH1	ARG E	25		81.285	35.435	10.379	1.00 90.12	7
	MOTA	6772	NH2	ARG E	25		82.938	33.892	9.880	1.00 97.12	6
		6773	C	ARG E			75.256	31.557	12.708	1.00 76.54	
	MOTA	6774	ō	ARG E			74.265	31.999	12.122	1.00 76.16	8
4.5	ATOM			PRO E			75.322	31.483	14.045	1.00 73.86	7
15	MOTA	6775	И	PRO E			76.343	30.778	14.834	1.00 73.05	6
	MOTA	6776	CD	PRO E			74.231	31.936	14.916	1.00 70.73	6
	MOTA	6777	CA				74.647	31.425	16.295	1.00 70.99	6
	MOTA	6778	СВ	PRO E			75.529	30.257	15.984	1.00 72.42	6
	MOTA	6779	CG	PRO E			74.199	33.466	14.891	1.00 67.63	6
20	MOTA	6780	С	PRO E				34.110	14.493	1.00 66.91	8
	MOTA	6781	0	PRO E			75.173	34.110	15.288	1.00 63.36	7
	ATOM	6782	N	VAL I			73.076		15.346	1.00 57.94	6
	MOTA	6783	CA	VAL I			72.980	35.487	15.266	1.00 55.79	6
	MOTA	6784	CB	VAL I			71.537	35.949	15.780	1.00 54.61	6
25	ATOM	6785		1 VAL	E 27		71.403	37.366		1.00 57.04	6
	MOTA	6786		2 VAL	E 27		71.082	35.870	13.839	1.00 57.83	6
	MOTA	6787		VAL			73.554	35.821	16.706	1.00 57.05	8
	MOTA	6788		VAL			73.180	35.207	17.711	1.00 56.05	7
		6789		ALA			74.490	36.760	16.744	1.00 55.79	6
00	MOTA	6790					75.087	37.130	18.014	1.00 55.59	
30	MOTA						76.508	37.588	17.810	1.00 54.25	6
	MOTA	6791		ALA			74.270	001	18.677	1.00 54.76	6
	MOTA	6792		ALA			74.244		18.216	1.00 54.28	8
	MOTA	6793					73.596		19.759	1.00 53.10	7
	MOTA	679		VAL			72.769			1.00 53.62	6
35	MOTA	679					71.338			1.00 52.63	6
	MOTA	679	6 CE				70.531			. 1.00 47.51 [.]	6
	MOTA	679	7 C	31 VAL	E 29						6
	ATOM	679	8 CC	32 VAL			70.641				6
	MOTA	679	9 C	VAL			73.412	_			8
40			0 0	VAL	E 29		73.760	_			7
	MOTA		1 N	SER	E 30		73.58				٠6
	ATOM			A SER	E 30		74.15				6
	ATOM				E 30		75.28				8
	ATOM	-					74.82				6
15							73.02	4 41.27			8
45							72.23				7
	MOTA				_		72.94	6 40.82	4 25.55		
	MOTA						71.93				6
	MOTA						71.05		8 26.96		6
	MOTA			B VAL G1 VAL	-		69.84		2 27.70		. 6
50	OTA (GI VAL) E 31		70.65			3 1.00 60.11	. 6
	IOTA	м 68		G2 VAI			72.59	-		4 1.00 61.00	6
	ATO	м 68	12 (.73.54			9 1.00 62.05	8
	ATO	м 68	13 0								. 7
	ATO!	м 68	14 P		RE 32		72.09				7 6
5				CA SE	RE 32		72.64				9 6
٥.	OTA				RE 32		73.68	38 44.74			
	OTA				RE 32	:	74.1	52 45.55			2 6
					RE 32	2	71.5		22 30.13		5 8
	ATO				RE 32		70.9	41 45.3			67
^	OTA O				UE 33		71.3	00 43.9			
6	O ATC				U E 33		70.2		91 32.1	65 1.00 56.6	∠ 0
	ATC	אס ניינע	321	تان در							

PCT/EP01/01457

	0 01,00									
						-184			4 4 6	_
	MOTA	6822	CB :	LEU E	33	69.658	43.578		1.00 54.43	6
	ATOM	6823		LEU E	33	69.031	42.344		1.00 55.79	6
	MOTA	6824		LEU E	33	68.247			1.00 53.82	6
	MOTA	6825		LEU E	33	68.132	42.781		1.00 56.32	6
5		6826	_	LEU E	33	70.880	45.717	32.985	1.00 56.68	6
3	ATOM		-	LEU E	33	71.954	45.572	33.556	1.00 58.07	8
	MOTA	6827	_	LYS E	34	70.186	46.843	33.029	1.00 55.71	7
	MOTA	6828			34	70.616	47.978	33.822	1.00 54.48	6
	MOTA	6829		LYS E		70.799	49.207	32.948	1.00 57.11	6
	MOTA	6830		LYS E	34	71.726	48.985	31.774	1.00 66.06	6
10	MOTA	6831		LYS E	34		48.679	32.205	1.00 71.51	6
	MOTA	6832		LYS E	34	73.179		30.973	1.00 73.37	6
	MOTA	6833		LYS E	34	74.103	48.409		1.00 72.80	7
	MOTA	6834	NZ	LYS E	34	75.541	48.135	31.351	1.00 72.00	6
	MOTA	6835	С	LYS E	34	69.459	48.201	34.776		8
15	MOTA	6836	0	LYS E	34	68.373	48.590	34.356	1.00 52.81	7
. •	ATOM	6837	N	PHE E	35	69.668	47.947	36.059	1.00 51.67	
	MOTA	6838	CA	PHE E	35	68.584	48.120	37.011	1.00 49.05	6
	MOTA	6839	СВ	PHE E	35	68.890	47.364	38.292	1.00 46.62	6
		6840	CG	PHE E	35	68.921	45.883	38.095	1.00 47.20	6
00	MOTA			PHE E	35	70.071	45.254	37.651	1.00 46.38	6
20	MOTA	6841		PHE E	35	67.766	45.125	38.253	1.00 49.08	6
	MOTA	6842			35	70.074	43.897	37.363	1.00 47.59	6
	MOTA	6843		PHE E		67.755	43.760	37.964	1.00 48.98	6
	MOTA	6844	CE2		35	68.913	43.145	37.517	1.00 48.13	6
	MOTA	6845	CZ	PHE E			49.560	37.285	1.00 48.83	6
25	MOTA	6846	С	PHE E		68.225	50.401	37.492	1.00 50.99	8
	MOTA	6847	0	PHE E		69.086		37.259	1.00 47.58	7
	MOTA	6848	N	ILE E	36	66.927	49.831		1.00 44.93	6
	MOTA	6849	CA	ILE E	36	66.403	51.166	37.465	1.00 44.37	6
	MOTA	6850	CB	ILE E	36	65.398	51.532	36.370	1.00 39.93	6
30	MOTA	6851	CG2	ILE E	36	64.927	52.956	36.547	1.00 35.33	6
- 00	MOTA	6852	CG1	ILE E	36	66.034	51.328	34.994	1.00 45.24	6
		6853		ILE E		67.290	52.114	34.776	1.00 46.74	
	MOTA	6854	C	ILE E		65.698	51.266	38.792	1.00 46.03	6
	MOTA			ILE E		65.588	52.350	39.347	1.00 46.58	8
05	MOTA	6855		ASN E		65.201	50.142	39.299	1.00 45.38	7
35	MOTA	6856		ASN I		64.510	50.163	40.580	1.00 44.10	6
	MOTA	6857				63.256		40.471	1.00 42.99	6
	MOTA	6858		ASN I		62.870		41.784	1.00 46.14	6
	MOTA	6859		ASN I		62.892		42.832	1.00 45.55	8
	MOTA	6860	OD:	1 ASN	E 37	62.497		41.731	1.00 45.29	7
40	MOTA	6861		2 ASN						6
	MOTA	6862	C C	ASN :		64.125				8
	MOTA	6863	3 0	ASN :		64.009				7
	MOTA	6864	ı N	ILE		63.951				6
	MOTA	6865	5 CA	ILE	E 38	63.537	47.453			6
45	MOTA	686	5 CB	ILE	E 38	64.646				6
	MOTA	686	7 CG	2 ILE	E 38	64.152			1.00 46.43	
	MOTA			1 ILE	E 38	65.848	3 46.561			6
•				1 ILE		67.10	9 46.207			6
	MOTA			ILE		62.34	5 47.902	43.879		6
E0	MOTA			ILE		62.50	4 48.619	44.855	1.00 49.04	8
50				LEU		61.15		43.466	1.00 49.65	7
	MOTA					59.90			1.00 51.44	6
	MOTA					-58.85			1.00 53.02	6
	ATOM					59.35				6
	MOTA		5 C							6
55	ATOM	687	6 CI	ol LEU	E 39	58.31				
	ATOM		7 CI	2 LEU		59.71				6
	ATOM			LEU		59.31				
	ATOM			LEU		58.79				
	MOTA					59.33	2 45.78			
60						58.78				
0(OTA C	_				57.35	7 44.54	9 45.96	0 1.00 58.59	, 0
	AIO									

ATOM ATOM ATOM ATOM ATOM ATOM ATOM	6884 6885 6886 6887			40 40 40	-185 56.377 54.960 54.697	45.178	45.718	1.00 64.95 1.00 68.54 1.00 70.88	6 6 8
ATOM ATOM ATOM ATOM ATOM ATOM	6884 6885 6886 6887	CD C	GLU E	40	54.960	45.178	45.718	1.00 68.54	6
ATOM ATOM ATOM ATOM ATOM ATOM	6884 6885 6886 6887	CD C	GLU E						
MOTA MOTA MOTA MOTA MOTA	6885 6886 6887	OE1 C	GLU E			44 405	44 555	1 00 70 98	0
MOTA MOTA MOTA MOTA	6886 6887					44.405			0
MOTA MOTA MOTA	6887	<u> </u>	TIII E	40	54.119		46.564	1.00 69.89	8
MOTA MOTA			GLU E	40	59,620	43.773	46.449	1.00 55.88	6
MOTA			GLU E	40	60.029		45.498	1.00 58.42	8
	6888						47.700	1.00 55.75	7
							48.021	1.00 55.46	6
								1.00 56.94	6
								1.00 58.11	6
								1.00 55.88	6
								1.00 55.20	6
		-						1.00 55.44	8
		_	-		-			1.00 55.58	7
								1.00 56.97	6
								1.00 55.95	6
							50.490	1.00 55.31	6
							51.267		8
								1.00 53.42	7
							50.241	1.00 59.68	6
		_					49.393	1.00 60.84	8
						38.255	51.398	1.00 61.29	7
						37.242	51.717	1.00 62.43	6
						37.721	52.857		6
						36.787	53.120	1.00 70.44	6
						37.358	54.094		6
						36.601	54.486	1.00 74.81	8
						38.557	54.460	1.00 74.43	8
					61.355	35.920	52.070	1.00 61.19	6
					61.977	34.861	51.958	1.00 58.53	8
					60.094	35.994	52.484		7
				44	59.330	34.809	52.852		6
				44	57.999	35.178			6
					57.197	33.897	53.812	1.00 63.01	6
				44	58.258	35.946			6
					58.852	35.088			6
					58.983	34.000		1.00 60.40	6
					59.114	32.774			8 7
			THR E	45	58.532				6
			THR E	45	58.149			1.00 57.28	
		СВ	THR E	45					6 8
		OG1	THR E	45.	57.189			1.00 55.94	6
	6925	CG2	THR E	45					6
	6926	С							8
	6927	0	THR E	45					7
			ASN E	46					6
	6929	CA	ASN E	€ 46				1 00 54 61	6
	6930	CB	ASN F	₹ 46				1.00 54.01	6
	6931	. CG					-		8
	6932								7
	6933	ND2							6
	6934	C	ASN I	€ 46					8
	6935	5 0	ASN I						7
ATOM	6936	5 N							6
ATOM									6
ATOM	6938	в св							6
ATOM									6
MOTA									8
						_			
MOTA	694	3 C	GLU	E 4/	00.18				
	ATOM ATOM ATOM ATOM ATOM ATOM ATOM ATOM	ATOM 6889 ATOM 6890 ATOM 6891 ATOM 6893 ATOM 6893 ATOM 6894 ATOM 6895 ATOM 6896 ATOM 6897 ATOM 6898 ATOM 6899 ATOM 6900 ATOM 6901 ATOM 6902 ATOM 6903 ATOM 6905 ATOM 6906 ATOM 6907 ATOM 6908 ATOM 6908 ATOM 6910 ATOM 6911 ATOM 6912 ATOM 6911 ATOM 6912 ATOM 6913 ATOM 6914 ATOM 6915 ATOM 6916 ATOM 6917 ATOM 6918 ATOM 6917 ATOM 6918 ATOM 6920 ATOM 6921 ATOM 6922 ATOM 6923 ATOM 6933 ATOM 6934	ATOM 6889 N ATOM 6890 CA ATOM 6891 CB ATOM 6894 C ATOM 6895 O ATOM 6896 N ATOM 6896 N ATOM 6897 CA ATOM 6897 CA ATOM 6900 OD1 ATOM 6901 ND2 ATOM 6903 O ATOM 6906 CB ATOM 6908 CD ATOM 6911 C ATOM 6911 C ATOM 6911 C ATOM 6912 O ATOM 6912 O ATOM 6913 N ATOM 6914 CA ATOM 6915 CB ATOM 6916 CB ATOM 6917 CG1 ATOM 6918 CD1 ATOM 6918 CD1 ATOM 6910 CB ATOM 6911 C ATOM 6912 O ATOM 6912 O ATOM 6914 CA ATOM 6915 CB ATOM 6915 CB ATOM 6916 CG2 ATOM 6917 CG1 ATOM 6918 CD1 ATOM 6918 CD1 ATOM 6910 C CG2 ATOM 6910 C CG2 ATOM 6911 C CG1 ATOM 6910 C CG1 ATOM 6910 C CG1 ATOM 6910 C CG1 ATOM 6910 C CG1 ATOM 6920 O ATOM 6920 O ATOM 6920 O ATOM 6921 N ATOM 6920 CA ATOM 6920 CB ATOM 6921 CG1 ATOM 6921 CG1 ATOM 6921 CG2 ATOM 6921 CG1 ATOM 6931 CG1	ATOM 6889 N VAL E ATOM 6890 CA VAL E ATOM 6891 CB VAL E ATOM 6891 CB VAL E ATOM 6893 CG2 VAL E ATOM 6893 CG2 VAL E ATOM 6894 C VAL E ATOM 6895 O VAL E ATOM 6896 N ASN E ATOM 6897 CA ASN E ATOM 6897 CA ASN E ATOM 6899 CG ASN E ATOM 6899 CG ASN E ATOM 6900 OD1 ASN E ATOM 6901 ND2 ASN E ATOM 6901 ND2 ASN E ATOM 6902 C ASN E ATOM 6903 O ASN E ATOM 6904 N GLU E ATOM 6905 CA GLU E ATOM 6907 CG GLU E ATOM 6907 CG GLU E ATOM 6908 CD GLU E ATOM 6910 OE2 GLU E ATOM 6910 OE2 GLU E ATOM 6911 C GLU E ATOM 6911 C GLU E ATOM 6912 O GLU E ATOM 6914 CA ILE E ATOM 6915 CB ILE E ATOM 6915 CB ILE E ATOM 6916 CG2 ILE E ATOM 6917 CG1 ILE E ATOM 6918 CD1 ILE E ATOM 6919 C ILE E ATOM 6910 C ILE E ATOM 6920 C ILE E ATOM 6921 N THR E ATOM 6920 C ILE E ATOM 6921 N THR E ATOM 6920 C ILE E ATOM 6921 N THR E ATOM 6920 C ILE E ATOM 6921 N THR E ATOM 6920 C ILE E ATOM 6920 C ILE E ATOM 6921 N THR E ATOM 6920 C ILE E ATOM 6921 N THR E ATOM 6920 C ILE E ATOM 6920 C ILE E ATOM 6921 N THR E ATOM 6920 C ILE E ATOM 6920 C ILE E ATOM 6920 C A ASN E ATOM 6930 C B ASN E ATOM 6	ATOM 6889 N VAL E 41 ATOM 6890 CA VAL E 41 ATOM 6891 CB VAL E 41 ATOM 6893 CG2 VAL E 41 ATOM 6893 CG2 VAL E 41 ATOM 6895 C VAL E 41 ATOM 6896 N ASN E 42 ATOM 6896 N ASN E 42 ATOM 6897 CA ASN E 42 ATOM 6898 CB ASN E 42 ATOM 6899 CG ASN E 42 ATOM 6900 OD1 ASN E 42 ATOM 6901 ND2 ASN E 42 ATOM 6901 ND2 ASN E 42 ATOM 6902 C ASN E 42 ATOM 6903 O ASN E 42 ATOM 6904 N GLU E 43 ATOM 6905 CA GLU E 43 ATOM 6906 CB GLU E 43 ATOM 6907 CG GLU E 43 ATOM 6909 OE1 GLU E 43 ATOM 6910 OE2 GLU E 43 ATOM 6910 OE2 GLU E 43 ATOM 6910 CC GLU E 43 ATOM 6910 CE GLU E 43 ATOM 6910 OE2 GLU E 43 ATOM 6910 OE2 GLU E 43 ATOM 6910 OE2 GLU E 43 ATOM 6910 TLE E 44 ATOM 6911 C GLU E 43 ATOM 6910 TLE E 44 ATOM 6911 C GLU E 43 ATOM 6910 TLE E 44 ATOM 6910 TLE E 45 ATOM 6920 TLE E 45 ATOM 6930 TLE E	ATOM 6889 N VAL E 41 59.876 ATOM 6890 CA VAL E 41 60.675 ATOM 6891 CB VAL E 41 62.802 ATOM 6893 CG2 VAL E 41 62.802 ATOM 6893 CG2 VAL E 41 62.802 ATOM 6894 C VAL E 41 59.925 ATOM 6895 O VAL E 41 59.925 ATOM 6896 N ASN E 42 60.042 ATOM 6897 CA ASN E 42 59.381 ATOM 6897 CA ASN E 42 59.381 ATOM 6899 CG ASN E 42 57.220 ATOM 6899 CG ASN E 42 57.696 ATOM 6890 OD1 ASN E 42 57.696 ATOM 6900 OD1 ASN E 42 57.696 ATOM 6901 ND2 ASN E 42 57.696 ATOM 6902 C ASN E 42 60.360 ATOM 6903 O ASN E 42 60.527 ATOM 6906 CB GLU E 43 61.014 ATOM 6907 CG GLU E 43 62.005 ATOM 6908 CD GLU E 43 64.066 ATOM 6910 OE2 GLU E 43 64.066 ATOM 6910 CC GLU E 43 64.982 ATOM 6911 C GLU E 43 64.982 ATOM 6912 O GLU E 43 61.355 ATOM 6914 CA ILE E 44 59.330 ATOM 6915 CB ILE E 44 57.999 ATOM 6916 CG2 ILE E 44 59.330 ATOM 6917 CGI ILE E 44 58.983 ATOM 6918 CD1 ILE E 44 58.983 ATOM 6910 CC ILE E 44 58.983 ATOM 6910 CC ILE E 44 58.983 ATOM 6920 O ILE E 44 58.983 ATOM 6920 O ILE E 44 58.983 ATOM 6920 C THR E 45 55.724 ATOM 6920 C THR E 45 55.9245 ATOM 6920 CA ASN E 46 60.972 ATOM 6930 CB ASN E 46 60.972 ATOM 6931 CG ASN E 46 60.972 ATOM 6932 CD THR E 45 55.724 ATOM 6933 ND2 ASN E 46 63.288 ATOM 6934 C ASN E 46 60.972 ATOM 6935 C ASN E 46 60.972 ATOM 6936 C C THR E 45 55.724 ATOM 6937 CA GLU E 47 55.583 ATOM 6939 CG GLU E 47 55.583 ATOM 6930 CB ASN E 46 61.255 ATOM 6930 CB ASN E 46 63.922 ATOM 6931 CG GLU E 47 55.583	ATOM 6889 N VAL E 41 59.876 43.454 ATOM 6890 CA VAL E 41 62.675 42.300 ATOM 6891 CB VAL E 41 62.677 42.301 ATOM 6892 CG1 VAL E 41 62.878 43.361 ATOM 6893 CG2 VAL E 41 59.925 41.520 ATOM 6895 O VAL E 41 59.925 41.520 ATOM 6896 N ASN E 42 60.042 40.204 ATOM 6897 CA ASN E 42 59.381 39.350 ATOM 6898 CB ASN E 42 57.220 38.135 ATOM 6898 CB ASN E 42 57.220 38.135 ATOM 6900 OD1 ASN E 42 57.220 38.135 ATOM 6901 ND2 ASN E 42 57.220 38.353 ATOM 6901 ND2 ASN E 42 55.948 38.499 ATOM 6902 C ASN E 42 60.360 38.222 ATOM 6903 O ASN E 42 60.360 38.222 ATOM 6904 N GLU E 43 61.014 38.255 ATOM 6905 CA GLU E 43 62.005 37.242 ATOM 6907 CG GLU E 43 62.005 37.242 ATOM 6907 CG GLU E 43 64.066 36.787 ATOM 6909 OE1 GLU E 43 66.010 36.601 ATOM 6910 OE2 GLU E 43 66.010 36.601 ATOM 6911 C GLU E 43 66.010 36.601 ATOM 6912 C GLU E 43 66.010 36.601 ATOM 6913 N LLE E 44 60.994 35.994 ATOM 6914 CA LLE E 44 59.330 34.809 ATOM 6915 CB LLE E 44 57.999 35.178 ATOM 6916 CC2 LLE E 44 57.197 33.897 ATOM 6917 CG LLE E 44 59.330 34.809 ATOM 6919 C LLE E 44 59.330 34.809 ATOM 6910 OE2 GLU E 43 66.010 36.601 ATOM 6911 C GLU E 43 61.355 35.920 ATOM 6912 N LLE E 44 59.330 34.809 ATOM 6913 N LLE E 44 59.330 34.809 ATOM 6919 C LLE E 44 59.330 34.809 ATOM 6910 CC2 LLE E 44 59.330 34.809 ATOM 6910 CC3 LLE E 44 59.330 34.809 ATOM 6910 CC3 LLE E 44 59.330 34.809 ATOM 6910 CC3 LLE E 44 59.330 34.600 ATOM 6910 CC3 LLE E 44 59.330 34.600 ATOM 6910 CC3 LLE E 44 59.330 34.600 ATOM 6920 O LLE E 44 59.114 32.774 ATOM 6921 N THR E 45 58.532 34.692 ATOM 6922 CA THR E 45 59.120 33.357 ATOM 6920 CB ASN E 46 60.313 34.000 ATOM 6921 N ASN E 46 60.313 34.000 ATOM 6920 CB ASN E 46 60.313 34.000 ATOM 6930 CB ASN E 46 60.313 37.792 ATOM 6930 CB ASN E 46 60.972 35.508 ATOM 6930 CB ASN E 46 60.973 35.	ATOM 6899 CA VAL E 41 59.876 43.454 47.700 ATOM 6890 CA VAL E 41 60.675 42.300 48.021 ATOM 6891 CB VAL E 41 62.807 42.732 48.550 ATOM 6892 CGI VAL E 41 62.802 41.547 49.107 ATOM 6893 CG2 VAL E 41 59.925 41.520 49.078 ATOM 6896 C VAL E 41 59.925 41.520 49.078 ATOM 6897 C VAL E 41 59.925 41.520 49.078 ATOM 6896 N ASN E 42 59.381 39.350 49.995 ATOM 6896 N ASN E 42 59.381 39.350 49.995 ATOM 6897 CA ASN E 42 59.381 39.350 49.995 ATOM 6898 CB ASN E 42 57.220 38.135 50.490 ATOM 6899 CG ASN E 42 57.696 37.306 51.267 ATOM 6890 CD ASN E 42 57.696 37.306 51.267 ATOM 6901 ND2 ASN E 42 55.948 38.499 50.526 ATOM 6902 C ASN E 42 60.360 38.222 50.241 ATOM 6904 N GLU E 43 60.360 38.222 50.241 ATOM 6905 CA GLU E 43 62.005 37.242 51.717 ATOM 6906 CB GLU E 43 62.005 37.242 51.717 ATOM 6907 CG GLU E 43 64.066 36.787 53.120 ATOM 6909 OE1 GLU E 43 66.010 36.601 54.486 ATOM 6910 OE2 GLU E 43 66.010 36.601 54.486 ATOM 6911 C GLU E 43 61.977 34.861 51.958 ATOM 6911 C GLU E 43 61.977 34.861 51.958 ATOM 6913 N ILE E 44 57.197 34.861 51.958 ATOM 6915 CB ILE E 44 57.999 35.178 53.536 ATOM 6916 CG2 ILE E 44 57.999 35.178 53.812 ATOM 6917 CG1 ILE E 44 57.999 35.178 53.536 ATOM 6917 CG1 ILE E 44 57.999 35.178 53.536 ATOM 6918 CD1 ILE E 44 57.999 35.178 53.536 ATOM 6917 CG1 ILE E 44 57.999 35.178 53.812 ATOM 6916 CG2 ILE E 44 57.999 35.178 53.812 ATOM 6917 CG1 ILE E 44 57.999 35.178 53.812 ATOM 6918 CD1 ILE E 44 57.999 35.178 53.812 ATOM 6910 C ILE E 44 57.999 35.178 53.812 ATOM 6910 C ILE E 44 57.999 35.178 53.812 ATOM 6920 C THR E 45 59.144 32.774 51.592 ATOM 6921 N THR E 45 59.143 33.332 48.932 ATOM 6920 C THR E 45 59.144 32.774 51.592 ATOM 6921 N THR E 45 59.144 32.774 51.592 ATOM 6922 CA THR E 45 59.144 32.774 51.592 ATOM 6923 CD THR E 45 59.144 32.774 51.592 ATOM 6926 C THR E 45 59.144 32.774 51.592 ATOM 6927 O THR E 45 59.145 34.696 48.710 ATOM 6933 ND2 ASN E 46 63.228 33.322 48.290 ATOM 6933 CG ASN E 46 63.228 33.322 48.290 ATOM 6933 CG ASN E 46 63.228 33.322 48.290 ATOM 6934 C ASN E 46 63.228 33.322 48.290 ATOM 6935 CG GLU E 47 59.769	ATOM 6899 N VAL E 41 59.876 43.454 47.700 1.00 55.76 ATOM 6891 CB VAL E 41 60.675 42.300 48.021 1.00 55.46 ATOM 6891 CB VAL E 41 62.807 42.732 48.550 1.00 55.46 ATOM 6892 CG1 VAL E 41 62.807 41.547 49.107 1.00 55.48 ATOM 6893 CG2 VAL E 41 59.925 41.520 49.078 1.00 55.88 ATOM 6894 C VAL E 41 59.925 41.520 49.078 1.00 55.88 ATOM 6895 N ASN E 42 59.936 41.520 49.078 1.00 55.58 ATOM 6897 CA ASN E 42 59.931 39.350 49.908 1.00 55.54 ATOM 6898 CB ASN E 42 59.931 39.350 49.908 1.00 55.54 ATOM 6899 CG ASN E 42 57.220 38.135 50.490 1.00 55.531 ATOM 6899 CB ASN E 42 57.220 38.135 50.490 1.00 55.31 ATOM 6900 DD1 ASN E 42 57.696 37.306 51.267 1.00 56.97 ATOM 6901 ND2 ASN E 42 55.948 38.499 50.526 1.00 53.42 ATOM 6902 C ASN E 42 60.360 38.222 50.241 1.00 59.68 ATOM 6905 CA GLU E 43 62.005 37.242 51.717 1.00 62.43 ATOM 6906 CB GLU E 43 62.005 37.242 51.717 1.00 62.43 ATOM 6906 CB GLU E 43 62.005 37.242 51.717 1.00 62.43 ATOM 6909 CD1 E 43 62.005 37.242 51.717 1.00 62.43 ATOM 6909 CD1 E 43 64.066 36.787 53.120 1.00 70.44 ATOM 6910 OD2 GLU E 43 64.066 36.787 53.120 1.00 70.44 ATOM 6910 CB GLU E 43 64.066 36.787 53.120 1.00 70.44 ATOM 6910 CD2 GLU E 43 64.982 38.557 54.460 1.00 74.81 ATOM 6910 CD2 GLU E 43 64.066 36.787 53.120 1.00 74.43 ATOM 6910 CD2 GLU E 43 64.066 36.787 53.120 1.00 74.43 ATOM 6910 CD2 GLU E 43 64.066 36.787 53.120 1.00 74.43 ATOM 6910 CD2 GLU E 43 64.066 36.787 53.120 1.00 70.44 ATOM 6911 C GLU E 43 64.982 38.557 54.460 1.00 74.43 ATOM 6912 C GLU E 43 64.066 36.787 53.120 1.00 70.44 ATOM 6913 C GLU E 43 64.066 36.787 53.120 1.00 70.44 ATOM 6910 CD2 GLU E 43 66.010 36.601 54.486 1.00 74.43 ATOM 6910 CD2 GLU E 43 66.010 36.601 54.486 1.00 74.43 ATOM 6910 CD2 GLU E 43 66.010 36.601 54.486 1.00 74.43 ATOM 6910 CD2 GLU E 43 66.010 36.601 54.486 1.00 75.13 ATOM 6900 CD3 CLU E 43 66.010 36.601 54.486 1.00 75.13 ATOM 6900 CD3 CLU E 44 58.983 34.000 51.608 1.00 60.00 ATOM 6900 CD3 CLU E 44 58.983 34.000 51.608 1.00 60.00 ATOM 6900 CD3 CLU E 44 59.300 34.899 52.855 1.00 65.75 ATOM 6930 C ANN E 46 63.603 33.322 48.99 1

PCT/EP01/01457

						-100				_
	MOTA	6944	0	GLU E	47	60.134	39.243	45.919	1.00 51.14	8
	MOTA		N '	VAL E	48	60.597	38.980	43.742	1.00 51.27	7
	ATOM		CA	VAL E	48	61.037	40.352	43.574	1.00 51.20	6
	ATOM	6947	CB	VAL E	48	62.554	40.402	43.276	1.00 52.39	6
5	ATOM			VAL E	48	63.000	41.822	43.081	1.00 54.32	6
·	ATOM	6949		VAL E	48	63.319	39.778	44.411	1.00 53.03	6
	ATOM	6950		VAL E	48	60.290	41.062	42.452	1.00 49.53	6
	MOTA	6951	_	VAL E	48	59.974	40.474	41.425	1.00 47.97	8
		6952		ASP E	49	60.005	42.334	42.669	1.00 47.94	7
10	MOTA			ASP E	49	59.335	43.146	41.680	1.00 48.29	6
10	MOTA	6953	CA	ASP E	49	58.107	43.795	42.290	1.00 49.64	6
	MOTA	6954	CB	ASP E	49	57.146	44.300	41.249	1.00 .50.04	6
	MOTA	6955				57.596	44.853	40.228	1.00 47.78	8
	MOTA	6956		ASP E	49	55.931	44.151	41.459	1.00 53.33	8
	MOTA	6957	-	ASP E	49		44.200	41.330	1.00 48.39	6
15	MOTA	6958	С	ASP E	49	60.373	45.101	42.118	1.00 48.55	8
	ATOM	6959	0	ASP E	49	60.644		40.140	1.00 48.88	7
	MOTA	6960	N	VAL E	50	60.950	44.085	39.718	1.00 48.55	6
	MOTA	6961	CA	VAL E	50	62.011	44.988		1.00 50.40	6
	ATOM	6962	CB	VAL E	50	63.353	44.220	39.707	1.00 49.66	6
20	MOTA	6963	CG1	VAL E	50	63.428	43.303	38.492		6
	MOTA	6964	CG2	VAL E	50	64.511	45.188	39.721	1.00 55.70	6
	MOTA	6965	С	VAL E	50	61.801	45.642	38.354	1.00 47.28	8
	MOTA	6966	0	VAL E	50	61.057	45.134	37.523	1.00 48.34	
	MOTA	6967	N	VAL E	51	62.467	46.777	38.144	1.00 45.37	7
25	MOTA	6968	CA	VAL E	51	62.407	47.540	36.896	1.00 43.25	6
25 .	MOTA	6969	СВ	VAL E	51	61.930	48.993	37.131	1.00 41.43	6
		6970		VAL E		62.118	49.820	35.865	1.00 39.28	6
	MOTA	6971	CG2			60.478	49.000	37.546	1.00 39.33	6
	MOTA	6972	C	VAL E		63.821	47.597	36.333	1.00 44.33	6
20	MOTA	6973	0	VAL E		64.764	47.841	37.078	1.00 46.78	8
30	MOTA		N	PHE E		63.978	47,383	35.029	1.00 43.60	7
	MOTA	6974		PHE E		65.304	47.416	34.430	1.00 41.93	6
	MOTA	6975	CA	PHE E		65.997	46.085	34.678	1.00 41.48	6
5	MOTA	6976	CB	PHE E		65.275	44.917	34.070	1.00 42.18	6
٥-	MOTA	6977	CG	PHE		65.486	44.566	32.745	1.00 41.86	6
35	MOTA	6978				64.347		34.809	1.00 43.51	6
	MOTA	6979		PHE E		64.784			1.00 42.36	6
	MOTA	6980		L PHE E		63.638			1.00 45.87	6
	MOTA	6981	CE2			63.859			1.00 43.76	6
	MOTA	6982	CZ	PHE I		65.239			1.00 44.18	6
40	MOTA	6983	С	PHE I		64.183			1.00 43.22	8
	MOTA	6984	0	PHE I					1.00 46.10	7
	MOTA	6985	N	TRP		66.384			1.00 47.08	6
	MOTA	6986	CA	TRP		66.466			1.00 46.54	6
	MOTA	6987		TRP :		67.367			40 05	6
45	MOTA	6988		TRP :		66.822				6
	MOTA	6989				67.510				6
	MOTA	6990	CE	2 TRP		66.616		31.471		6
	ATOM.	6991		3 TRP		68.804		_		6
	MOTA	6992		1 TRP	E 53	65.577				7
50	MOTA	6993		1 TRP		65.440				6
- 00	MOTA	6994	CZ	2 TRP	E 53	66.969				6
	ATOM	6995				69.162				
	ATOM	6996		2 TRP		68.24	5 54.658			6
	MOTA	6997		TRP		67.07				6
55		6998		TRP		68.20				8
55				GLN		66.31	3 46.342			7
	MOTA					66.80				6
	MOTA					65.64		3 28.51	7 1.00 50.24	6
	MOTA					66.07		7 28.01	7 1.00 52.86	6
60	MOTA					65.04		8 28.31		6
60				E1 GLN		64.66		4 29.46	5 1.00 59.29	8
	MOTA	700	- OI	استن تت		2				

-186

PCT/EP01/01457

						-187				_
	MOTA	7005	NE2	GLN E	54	64.576	41.078	27.275	1.00 58.15	7
	ATOM	7006	C	GLN E	54	67.500	45.583	27.547	1.00 50.68	6
	MOTA	7007	ō	GLN E	54	66.972	45.458	26.446	1.00 50.31	8
	MOTA	7008	N	GLN E	55	68.692	46.132	27.735	1.00 53.08	7 6
5	MOTA	7009	CA	GLN E	55	69.534	46.620	26.647	1.00 55.55	6
_	MOTA	7010	СВ	GLN E	55	70.723	47.342	27.257	1.00 57.75 1.00 65.99	6
	MOTA	7011	CG	GLN E	55	71.798	47.759	26.296	1.00 65.99	6
	MOTA	7012	CD	GLN E	55	72.759	48.745	26.952 28.158	1.00 76.80	8
	MOTA	7013	OE1		55	73.057	48.637	26.175	1.00 70.33	7
10	MOTA	7014	NE2	GLN E	55	73.245 69.978	49.710 45.446	25.768	1.00 54.06	6
	MOTA	7015	C	GLN E	55	70.834	44.648	26.147	1.00 55.16	8
	MOTA	7016	0	GLN E		69.370	45.350	24.592	1.00 51.47	7
	MOTA	7017	N	THR E		69.638	44.266	23.664	1.00 49.57	6
4 =	MOTA	7018	CA CB	THR E	_	68.340	43.527	23.323	1.00 48.99	6
15	MOTA	7019 7020		THR E		67.621	43.259	24.530	1.00 51.03	8
	MOTA	7020		THR E		68.638	42.228	22.613	1.00 48.81	6
	ATOM ATOM	7021	C	THR E		70.245	44.780	22.374	1.00 48.56	6
	ATOM	7023	Õ	THR E		69.919	45.870	21.916	1.00 47.42	8
20	ATOM	7024	N	THR E		71.131	43.984	21.789	1.00 48.33	7 6
20	MOTA	7025	CA	THR E		71.778	44.370	20.545	1.00 48.63	6
	ATOM	7026	CB	THR E		73.079	45.153	20.803	1.00 48.38 1.00 49.73	8
	MOTA	7027		THR E		72.786	46.369	21.504	1.00 49.73	6
	MOTA	7028	CG2	THR F		73.737	45.498	19.488 19.688	1.00 47.10	6
25	MOTA	7029	С	THR I		72.115	43.162	20.196	1.00 47.16	8
	MOTA	7030	0	THR F		72.462	42.094 43.337	18.382	1.00 44.64	7
	MOTA	7031	N	TRP I		71.996 72.302	42.272	17.443	1.00 45.43	6
	MOTA	7032	CA	TRP I		71.217	41.185	17.463	1.00 44.32	6
	MOTA	7033		TRP I	_	69.901	41.590	16.907	1.00 41.75	6
30	MOTA	7034		TRP : 2 TRP :		68.834	42.225	17.617	1.00 41.25	6
	MOTA	7035				67.800	42.458	16.689	1.00 43.06	6
	MOTA	7036 7037				68.653	42.622	18.948	1.00 42.08	6
	MOTA MOTA	7037				69.485	41.463	15.622	1.00 39.77	6 7
35	MOTA	7039				68.229		15.477	1.00 43.20	6
00	MOTA	7040				66.598		17.043	1.00 42.98 1.00 45.88	6
	MOTA	7041			E 58	67.462		19.301	1.00 45.88	6
	MOTA	7042	2 CH			66.447		18.347 16.060	1.00 46.92	6
	MOTA	7043	3 C	TRP		72.450			46 00	8
40	MOTA	704	4 0	TRP		72.312				7
	MOTA	704		SER	_	72.737 72.933				6
	MOTA	704				74.423			1.00 55.16	6
	MOTA				_	74.777			1.00 59.85	8
4	MOTA			SER SER	_	72.093			1.00 53.08	6
45				SER	0	72.023		12.621	1.00 50.22	8
	MOTA MOTA			ASP		71.46	1 42.685	11.833		7
	ATOM					70.61	6 42.206			6
	MOTA					69.14	4 42.502			6 6
50					E 60	68.21				8
	ATOM		5 0	D1 ASP		68.62				8
	ATOM		6 0	D2 ASP		67.06				6
	ATOM			ASP	E 60	71.04				8
	ATOM	1 705	8 O			70.59				7
55						71.89 72.42		_	1 1.00 66.18	6
	OTA			A ARG		73.58		_	8 1.00 70.24	6.
	OTA			B ARG		74.95			6 1.00 74.18	6 '
	OTA			G ARG		76.04			2 1.00 80 <i>.</i> 58	6
e.	OTA			D ARC IE ARC		77.41		5 7.22		7
60	IOTA C IOTA		-	Z ARC				7 6.59	8 1.00 88.23	6
	AIU									

PCT/EP01/01457

						•00				
						-188	40 734	5.447	1.00 88.94	7
	MOTA	7066	NH1 A		61	78.383	40.734	7.111	1.00 88.58	7
	MOTA	7067	NH2 A		61	79.724 71.404	43.289	6.414	1.00 65.48	6
	MOTA	7068	_	ARG E	61	71.655	44.145	5.561	1.00 65.84	8
_	MOTA	7069	_	ARG E	61	70.255	42.610	6.439	1.00 64.00	7
5	MOTA	7070		THR E	62 62	69.232	42.842	5.410	1.00 61.93	6
	MOTA	7071		THR E THR E	62	68.113	41.764	5.439	1.00 62.28	6
	ATOM	7072 7073		THR E	62	67.367	41.879	6.652	1.00 65.24	8
	MOTA	7074		THR E	62	68.707	40.361	5.372	1.00 61.73	6
10	MOTA MOTA	7075		THR E	62	68.602	44.218	5.595	1.00 59.03	6
10	ATOM	7076		THR E	62	67.827	44.676	4.761	1.00 57.27	8
	MOTA	7077		LEU E	63	68.962	44.868	6.697	1.00 57.62	7 6
	ATOM	7078		LEU E	63	68.461	46.200	7.029	1.00 57.37	6
	MOTA	7079		LEU E	63	68.214	46.316	8.543	1.00 55.66 1.00 55.07	6
15	ATOM	7080		LEU E	63	67.253	45.322	9.196	1.00 52.03	6
	MOTA	7081		LEU E	63	67.231		10.692	1.00 55.09	6
	MOTA	7082		LEU E	63	65.875	45.519	8.612 6.625	1.00 57.97	6
	ATOM	7083		LEU E	63	69.471	47.277 48.460	6.549	1.00 56.59	8
	MOTA	7084	-	LEU E	63	69.135	46.862	6.389	1.00 58.86	7
20	MOTA	7085		ALA E	64	70.715 71.770	47.798	6.018	1.00 60.30	6
	MOTA	7086		ALA E	64	73.077	47.055	5.844	1.00 58.52	6
	MOTA	7087	СВ	ALA E	64 64	71.440	48,571	4.745	1.00 61.25	6
	MOTA	7088	C	ALA E	64	70.814	48.041	3.830	1.00 59.01	8
0.5	MOTA	7089	N	TRP E	65	71.845	49.832	4.702	1.00 63.42	7
25	MOTA	7090 7091	CA	TRP E	65	71.619	50.631	3.514	1.00 67.05	6
	MOTA	7091	CB	TRP E	65	70.406	51.537	3.704	1.00 66.45	6
	MOTA	7092	CG	TRP E	65	70.513	52.506	4.835	1.00 66.84	6
	ATOM ATOM	7094		TRP E		70.173	_. 52.266	6.209	1.00 67.35	6 6
30	ATOM	7095		TRP E		70.352	53.488	6.904	1.00 67.71	6
50	ATOM	7096		_		69.730	51.141	6.920	1.00 65.56 1.00 66.32	6
	MOTA	7097	CD1	TRP E	65	70.882	53.816	4.756	1.00 67.91	7
	ATOM	7098	NE1	TRP E	65	70.785		5.993 8.270	1.00 65.59	6
	ATOM	7099	CZ2	TRP E		70.101		8.272	1.00 64.14	6
35	MOTA	7100	CZ3			69.483		8.935	1.00 65.02	6
	MOTA	7101		TRP E		69.668		3.253		6
	MOTA	7102		TRP E		72.874 73.908		3.902		8
	MOTA	7103		TRP E		72.801		2.297	1.00 71.64	7
	MOTA	7104		ASN E	_	73.956		1.999	1.00 72.49	6
40	ATOM	7105		ASN I		74.174		0.486		6
	MOTA	7106		ASN I		75.497		0.131		6
	ATOM	7107 7108		L ASN		75.513		-0.456	1.00 76.49	8
	MOTA			2 ASN		76.61	4 53.347	0.487		7
45	MOTA				E 66	73.70	7 54.561	2.602		6
43	MOTA MOTA			ASN		72.93	0 55.361	2.068		8 7
	ATOM			SER		74.36		3.726		6
	MOTA					74.23		4.441		6
	ATOM					74.15		5.942	4	8
50					E 67	75.16		6.30		6
	MOTA			SER		75.37		4.15° 4.80°		8
	ATOM		7 0	SER		75.51	2 58.093			
	ATOM		и 8.	SER		76.19				6
	ATOM	711				77.35				
55	MOTA					78.21			04 00	8
	MOTA					77.53 76.89				6
	1OTA	4 712		SER		77.58			1 1.00 79.89	8
	MOTA			SER		75.72		_	4 1.00 77.21	. 7
-	OTA			RIH RIH A		75.17		2.24	7 1.00 76.33	6
60						75.22			2 1.00 76.74	. 6
	ATO	M 712	26 CE	ט דט	_ 05					

	***************************************	,,,,,								
						-189	-			_
	MOTA	7127	CG I	HIS E	69	75.366	62.083	0.283	1.00 77.46	6
	ATOM	7128		HIS E	69	74.568	62.857 -	-0.491 :	1.00 76.01	6
	ATOM	7129		HIS E	69	76.390	62.898	0.720	1.00 75.50	7
	ATOM	7130		HIS E	69	76.212	64.114		1.00 74.91	6
5	ATOM	7131		HIS E	69	75.115	64.117	-0.497	1.00 77.04	7
•	MOTA	7132		HIS E	69	73.748	60.641		1.00 75.96	6
	MOTA	7133	_	HIS E	69	72.954	61.408	2.170	1.00 75.96	8 7
	ATOM	7134	-	SER E	70 .	73.431	59.880		1.00 75.27	6
	ATOM	7135		SER E	70	72.086	59.867		1.00 72.77	6
10	ATOM	7136	СВ	SER E	70	71.307	58.758		1.00 71.14	8
.0	MOTA	7137	OG	SER E	70	72.085	57.578		1.00 68.45	6
	ATOM	7138	С	SER E	70	72.177	59.585		1.00 72.84 1.00 73.59	8
	ATOM	7139	0	SER E	70	73.254	59.212		1.00 73.33	7
	ATOM	7140	N	PRO E	71	71.065	59.789	6.550	1.00 71.63	6
15	ATOM	7141	CD	PRO E	71	69.793	60.434	6.160	1.00 70.03	6
. •	ATOM	7142	CA	PRO E	71	71.091	59.521	7.989	1.00 69.50	6
	MOTA	7143	CB	PRO E	71	69.627	59.649	8.376	1.00 69.75	6
	ATOM	7144	CG	PRO E	71	69.172	60.783	7.505	1.00 67.45	6
	ATOM	7145	С	PRO E	71	71.611	58.104	8.128	1.00 67.47	8
20	ATOM	7146	0	PRO E	71	71.371	57.288	7.249 9.202	1.00 65.90	7
-•	MOTA	7147	N	ASP E	72	72.332	57.813	9.202	1.00 65.38	6
	ATOM	7148	CA	ASP E	72	72.888	56.480	9.401	1.00 66.99	6
	ATOM	7149	CB	ASP E	72	74.336	56.595	10.513	1.00 69.68	6
	MOTA	7150	CG	ASP E	72	74.623	57.933	10.511	1.00 72.85	8
25	MOTA	7151		ASP E	72	75.809	58.349 58.564	11.022	1.00 69.14	8
	MOTA	7152	OD2	ASP E	72	73.659	55.656	10.387	1.00 64.69	6
	MOTA	7153	С	ASP E		72.078	54.438	10.492	1.00 62.72	8
	MOTA	7154	0	ASP E		72.273 71.194	56.334	11.122	1.00 63.38	7
	MOTA	7155	N	GLN E		70.291	55.692	12.073	1.00 62.59	6
30	MOTA	7156	CA	GLN E		70.703	55.968	13.502	1.00 63.56	6
	MOTA	7157		GLN E		71.812		14.064	1.00 66.36	6
	MOTA	7158		GLN E		72.073		15.478	1.00 69.74	6
	ATOM	7159	_	GLN E		72.311		15.711	1.00 71.52	8
	MOTA	7160				72.005		16.437	1.00 70.16	7
35	ATOM	7161		GLN E		68.850		11.932	1.00 60.94	6
	MOTA	7162		GLN I		68.599		11.548	1.00 60.74	8
	MOTA	7163		VAL I		67.910		12.281	1.00 57.54	7
	MOTA	7164				66.495		12.254	1.00 54.00	6
40	ATOM	7165		_		65.857		10.901	1.00 52.88	6
40	ATOM	7166		1 VAL		66.393		9.814	1.00 52.07	6
	MOTA	7167 7168		2 VAL		66.153		10.564	1.00 53.11	6 6
	MOTA	716		VAL		65.81	54.844	13.349	1.00 51.46	8
	MOTA MOTA	717		VAL		66.35		13.804	1.00 51.44	7
45				SER		64.64		13.789		6.
40	MOTA					63.89	3 54.592			6
	MOTA				E 75	63.22	2 55.583			8
	MOTA					64.12	2 56.022			6
	MOTA			SER	E 75	62.84	6 53.727			8
50				SER		61.95	9 54.228	13.431	44 00	7
00	ATOM			VAL	E 76	62.95				
	ATOM	_		AAV AL		62.05				
	ATOM		9 CI	B VAL		62.85				6
	ATOM		30 C	31 VAL	E 76	61.93				6
55		_	31 C	G2 VAL	E 76	63.73				. 6
	ATOM		32 C			61.16				8
	ATO		33 O			61.64				
	ATOM		34 N			59.86				6
	ATO					59.08			0 1.00 39.46	5 6
60	iota 0			A PRO		58.98 57.6	·			3 6
	ATO	M 71	87 C	B PRO	E 77	5/.0.	٠٠.٥٠			

							-190				_
	MOTA	7188	CG	PRO E	3 7	7	57.736			1.00 41.25	6
	ATOM	7189	C	PRO E		7	59.407			1.00 39.33	6
	ATOM	7190	Ō	PRO I	s 7	7	59.766			1.00 39.91	8 7
	ATOM	7191	N	ILE I	≅ 7	8	59.368	47.929	16.665	1.00 39.53	6
5	ATOM	7192	CA	ILE 1	E 7	8	59.729	46.550		1.00 39.36 1.00 41.90	6
	MOTA	7193	CB	ILE :		8	59.440	46.235	18.408	1.00 41.90	6
	MOTA	7194	CG2	ILE :		8	59.421	44.753	18.667	1.00 45.61	6
	MOTA	7195	CG1	ILE		8	60.512	46.887	19.259 18.783	1.00 45.82	6
	MOTA	7196	CD1	ILE		8	61.904	46.569	16.048	1.00 39.58	6
10	MOTA	7197	С	ILE		78	59.002	45.562 44.550	15.645	1.00 39.79	8
	ATOM	7198	0	ILE		78	59.556	45.870	15.729	1.00 41.50	7
	MOTA	7199	N	SER		79	57.755 56.932	45.011	14.891	1.00 41.99	6
	MOTA	7200	CA	SER		79	55.497	45.502	14.931	1.00 40.86	6
	MOTA	7201	CB	SER		79	55.441	46.876	14.633	1.00 44.60	8
15	MOTA	7202	OG	SER		79 79	57.370	44.887	13.441	1.00 43.24	6
	ATOM	7203	C	SER		79	56.883	44.020	12.730	1.00 43.62	8
	MOTA	7204	0	SER SER		80	58.278	45.750	12.996	1.00 44.61	7
	MOTA	7205	N	SER		80	58.751	45.713	11.619	1.00 44.15	6
00	MOTA	7206	CA	SER		80	58.841	47.133	11,062	1.00 43.26	6
20	MOTA	7207	CB OG	SER		80	57.568	47.744	11.017	1.00 47.92	8
	MOTA	7208 7209	C	SER		80	60.110	45.033	11.482	1.00 45.19	6
	MOTA MOTA	7210	Ö	SER		80	60.661	44.963	10.387	1.00 46.20	8
	ATOM	7211	N.	LEU		81	60.645	44.533	12.589	1.00 42.25	7
25	MOTA	7212	CA	LEU		81	61.949	43.891	12.577	1.00 42.76	6
20	ATOM	7213	CB	LEU		81	62.950	44.702	13.400	1.00 41.44	6 6
	ATOM	7214		LEU		81	63.144		13.150	1.00 39.51 1.00 38.48	6
	MOTA	7215		1 LEU	E	81	63.861		14.314	1.00 43.00	6
	ATOM	7216		2 LEU	E	81	63.908		11.891	1.00 42.93	6
30	MOTA	7217		LEU		81	61.846		13.216	1.00 47.16	8
	MOTA	7218	0	LEU		81	60.845		13.865 13.028	1.00 39.63	7
	ATOM	7219	N	TRP		82	62.880		13.657	1.00 38.60	6
	ATOM	7220	CA			82	62.925		12.941	1.00 37.23	6
	MOTA	7221				82	63.872 64.186		13.753	1.00 39.34	6
35	MOTA	7222				82	65.272		14.678	1.00 41.49	6
	MOTA	7223		2 TRE		82 82	65.142		15,266	1.00 40.40	6
	MOTA	7224				82	66.34		15.071	1.00 41.39	6
	MOTA	7225	CE	3 TRI		82	63.46		13.814	1.00 37.83	6
40	ATOM	7220		1 TRI	- E	82	64.03		14.719	1.00 40.75	7
40	MOTA	722 722		2 TR		82	66.04	4 36.335			6
	MOTA	722				82	67.23	7 38.436	16.025	1.00 38.98	6
	MOTA MOTA		_		PΕ	82	67.08	0 37.161	16.591		6
	ATOM		-		PΕ	82	63.51				6 8
45		_			PΕ	82	64.35		15.086		7
~	MOTA			VA	LΕ	83	63.06				6
	ATOM				LΕ	83	63.57				6
	ATOM		5 C	B VA	LΕ	83	62.56				6
	ATOM		6 C	G1 VA		83	62.91				6
50			7 C	G2 VA	LΕ	83	62.55				6
	ATOM		8 C		LΕ	83	63.85				
	ATOM	1 723	9 0		L E	83	63.15				7
	ATOM				OE	84	64.90				6
	MOTA				OE	84	65.92 65.2				6
55	OTA 6				10 E	84					
	1OTA				80 E	84	66.41 67.0			0 1.00 37.91	. 6
	OTA				RO E		64.1			5 1.00 36.04	6
	ATO				RO E		63.5			6 1.00 34.75	8
_	ATO			ום כ זיי די	RO E	84	63.8			5 1.00 33.87	
6		_			SP E	85	62.7				5 6
	OTA	м 72	48 (CA A	סב ב	, 05	02.7				

	W O 01/50	9231								
						-191				_
	ATOM	7249	CB A	SP E	85	62,150			1.00 37.18	6
	ATOM			SP E	85	63.150	33.259	20.556	1.00 40.21	6
	ATOM		OD1 A		85	64.268			1.00 41.52	8
	ATOM		OD2 A		85	62.828			1.00 38.39	8
5	ATOM	7253		ASP E	85	63.277		22.794	1.00 36.88	6
0	MOTA	7254		ASP E	85	63.139	•		1.00 37.96	8
	MOTA	7255		LEU E	86	63.848	36.307		1.00 34.95	7
	MOTA	7256		LEU E	86	64.387 -		-	1.00 36.75	6
	ATOM	7257		LEU E	86	65.211	37.414		1.00 36.06	6 6
10	MOTA	7258		LEU E	86	66.410	37.646		1.00 34.31	6
. •	ATOM	7259		LEU E	86	67.131	38.893	24.653	1.00 32.72 1.00 35.49	6
	ATOM	7260	CD2	LEU E	86	67.300	36.446	24.287	1.00 35.49	6
	ATOM	7261	С	LEU E	86	63.317	36.021	25.816	1.00 37.01	8
	ATOM	7262	0	LEU E	86	62.226	36.557	25.694	1.00 41.31	7
15	ATOM	7263	N	ALA E	87	63.652	35.293	26.865	1.00 30.35	6
	MOTA	7264		ALA E	87	62.727	35.060	27.949	1.00 37.37	6
	MOTA	7265		ALA E	87	61.950	33.766	27.692 29.255	1.00 41.61	6
	MOTA	7266	C	ALA E	87	63.510	34.959 34.372	29.288	1.00 42.91	8
	MOTA	7267	0	ALA E	87	64.583	34.372	30.323	1.00 41.72	7
20	MOTA	7268	N	ALA E	88	62.989	35.460	31.624	1.00 40.16	6
	MOTA	7269	CA	ALA E	88	63.639	36.638	32.480	1.00 38.02	6
	MOTA	7270	CB	ALA E	88	63.259	34.168	32.261	1.00 41.60	6
	MOTA	7271	С	ALA E	88	63.154 62.028	34.189	32.740	1.00 43.75	8
	MOTA	7272	0	ALA E	88	64.008	33,152	32.245	1.00 43.12	7
25	MOTA	7273	N	TYR E	89	63.691	31.832	32.793	1.00 44.73	6
	MOTA	7274	CA	TYR E	89	64.970	31.010	32.900	1.00 47.55	6
	MOTA	7275	CB	TYR E		65.633	30.711	31.573	1.00 53.63	6
	MOTA	7276	CG	TYR E		66.903	30.120	31.521	1.00 54.69	6
	MOTA	7277		TYR E		67.519	29.831	30.311	1.00 56.44	6
30	MOTA	7278	CEI	TYR E	89	64.995	31.006	30.368	1.00 56.01	6
	MOTA	7279		_		65.599	30.720	29.147	1.00 58.87	6
	MOTA	7280	CE2	TYR E		66.860	30.131	29.125	1.00 58.82	6
	MOTA	7281 7282	OH	TYR E		67.437	29.821	27.908	1.00 64.15	8
25	MOTA	7283	C	TYR E		62.959	31.792	34.138	1.00 44.61	6 8
35	MOTA MOTA	7284		TYR E		62.113	30.920	34.362	1.00 43.17	7
	MOTA	7285		ASN I		63.275		35.036	1.00 43.58 1.00 43.92	6
	ATOM	7286		ASN I		62.621	32.729	36.338	1.00 41.30	6
	MOTA	7287		ASN I		63.658		37.469	1.00 40.93	6
40	MOTA	7288		ASN I	∃ 90	64.654		37.401	1.00 40.18	8
70	ATOM	7289		L ASN	E 90	65.197			1.00 42.13	7
	MOTA	7290	ND:	2 ASN	E 90	64.914			1.00 45.22	6
	ATOM	7291	L C	ASN	E 90	61.668				8
	ATOM		2 0	ASN		61.397				7
45	MOTA		3 N	ALA		61.170				6
	MOTA					60.207				6
	MOTA	7299				59.974 58.93				6
	MOTA			ALA		58.54				8
	MOTA			ALA		58.30				7
50	MOTA (ILE		57.11			1.00 45.40	6
	ATOM					57.30			1.00 49.00	6
	ATOM					56.51			3 1.00 53.30	6
	MOTA		1 CG			56.88			1.00 50.53	6
	MOTA		2 CG	1 ILE	E 92	56.90			9 1.00 57.12	
55				1 ILE	_	55.86			0 1.00 43.27	
	MOTA			ILE		54.74		8 37.39		. 8
	ATO1			SER		56.07		6 36.21		. 7
	MOTA.					55.00				5 6
e	IOTA					54.76	38.86			
6						55.84	9 39.75	6 36.17	0 1.00 40.42	8 8
	OTA	r. /30	,,							

```
-192
                      7310 C SER E 93 55.497 37.925 34.214 1.00 41.98
7311 O SER E 93 56.686 37.781 33.932 1.00 43.61
7312 N LYS E 94 54.617 38.380 33.333 1.00 41.47
7313 CA LYS E 94 55.109 38.738 32.018 1.00 44.98
7314 CB LYS E 94 52.663 39.071 31.264 1.00 48.24
7315 CG LYS E 94 52.663 39.071 31.264 1.00 48.24
7316 CD LYS E 94 52.173 38.628 28.822 1.00 50.47
7317 CE LYS E 94 51.659 38.499 30.255 1.00 50.47
7318 NZ LYS E 94 51.218 38.125 27.795 1.00 54.79
7319 C LYS E 94 55.675 40.151 32.031 1.00 45.16
7320 O LYS E 94 55.386 40.939 32.933 1.00 46.22
7321 N PRO E 95 56.514 40.481 31.038 1.00 43.95
7322 CD PRO E 95 56.973 39.633 29.926 1.00 42.19
7323 CA PRO E 95 56.973 39.633 29.926 1.00 42.19
7324 CB PRO E 95 58.306 40.216 29.636 1.00 42.27
7325 CG PRO E 95 56.162 42.939 30.761 1.00 42.70
7326 C PRO E 95 56.162 42.939 30.761 1.00 42.70
7327 O PRO E 95 55.320 42.899 29.870 1.00 42.27
7328 N GLU E 96 55.424 45.115 31.446 1.00 41.45
7330 CB GLU E 96 53.911 46.797 32.674 1.00 40.32
7331 CG GLU E 96 53.911 46.797 32.674 1.00 47.98
7333 OE1 GLU E 96 53.911 46.797 32.674 1.00 47.98
7333 OE1 GLU E 96 53.911 46.797 32.674 1.00 47.98
7334 OE2 GLU E 96 53.482 46.539 35.005 1.00 53.57
7338 CA VAL E 97 57.200 47.165 28.800 1.00 34.15
7339 CB VAL E 97 57.200 47.165 28.800 1.00 34.15
7339 CB VAL E 97 57.200 47.165 28.800 1.00 34.15
7344 CG2 VAL E 97 57.08 45.444 27.113 1.00 28.98
7345 C VAL E 97 57.708 45.444 27.113 1.00 28.98
7346 CG1 VAL E 97 57.665 48.576 29.041 1.00 35.79
7343 O VAL E 97 57.708 45.444 27.113 1.00 28.98
                                                                            55.497 37.925 34.214 1.00 41.98
                       7310 C SER E 93
7311 O SER E 93
7312 N LYS E 94
         MOTA
                                                                    56.686 37.781 33.932
         MOTA
         MOTA
         MOTA
 5
         MOTA
         MOTA
         MOTA
          MOTA
          MOTA
10
          MOTA
                                                                                                                                                           8
          MOTA
                                                                                                                                                           7
          MOTA
                                                                                                                                                           6
          MOTA
                                                                                                                                                           6
          MOTA
15
          MOTA
                                                                                                                                                           6
          MOTA
                                                                                                                                                           6
          MOTA
                                                                                                                                                           8
           MOTA
                                                                                                                                                           7
           MOTA
20
           MOTA
                                                                                                                                                           б
           MOTA
                                                                                                                                                            6
           MOTA
                                                                                                                                                            6
           MOTA
           MOTA
 25
           MOTA
           MOTA
           MOTA
                                                                                                                                                            7
            MOTA
            MOTA
 30
            MOTA
                                                                                                                                                             6
            MOTA
                                                                                                                                                             6
                          7341 CG2 VAL E 97
7342 C VAL E 97
7343 O VAL E 97
7344 N LEU E 98
            ATOM
            MOTA
                                                                               55.558 48.932 28.636
57.474 49.378 29.714
57.091 50.725 30.086
                                                                                                                                  1.00 35.88
                                                                                                                                                            8
            MOTA
                                                                                                                                  1.00 35.63
  35
            MOTA
                                                                                                                                 1.00 36.41
                                                                               57.091 50.725 30.086
57.787 51.098 31.395
                           7345 CA LEU E 98
             MOTA
                                                                                                                                 1.00 34.14
                                       CB LEU E 98
                           7346
                                                                               57.676 50.176 32.598 1.00 33.56
             MOTA
                                                                                                                                                              6
                                      CG LEU E 98
CD1 LEU E 98
CD2 LEU E 98
                                                                               58.694 50.570 33.602 1.00 31.56
56.306 50.248 33.190 1.00 33.37
57.400 51.793 29.058 1.00 36.97
56.969 52.936 29.203 1.00 38.13
                           7347
             MOTA
                                                                                                                                                              6
                           7348
             MOTA
                            7349
  40
             MOTA
                                               LEU E 98
             MOTA
                           7350
                                       C
                                                                                                                                                              8
                                       O LEU E 98
N THR E 99
CA THR E 99
CB THR E 99
                            7351
                                                                                                                                 1.00 35.68
             MOTA
                                                                                58.133 51.426 28.018
                            7352 N
             MOTA
                                                                                                                                  1.00 34.41
                                                                                58.533 52.391 27.011
                            7353
                                                                                60.067 52.547 27.032
60.683 51.265 26.850
60.517 53.122 28.355
             MOTA
                                                                                                                                  1.00 35.73
                                                                                                                                                               6
   45
             MOTA
                            7354
                                                                                                                                  1.00 39.59
                                        OG1 THR E 99
              MOTA
                            7355
                                                                                                                                  1.00 34.05
                                                                                                                                                               6
                                        CG2 THR E 99
                            7356
              MOTA
                                                                                                                                  1.00 33.50
                                                                                                                                                               6
                                                                                 58.098 52.084 25.589
                                                 THR E 99
THR E 99
PRO E 100
                            7357
                                        C
             MOTA
                                                                                                                                  1.00 33.37
                                                                                                                                                               8
                                                                                57.696 50.969 25.283
                                                                                                                                  1.00 34.01
                            7358
                                        0
              MOTA
                                                                               58.155 53.093 24.701
58.424 54.514 24.975
57.777 52.919 23.302
   50
                            7359
                                         N
              MOTA
                                                                                                                                   1.00 36.06
                                         CD PRO E 100
              MOTA
                             7360
                                                                                                                                  1.00 33.45
                             7361 CA PRO E 100
                                                                                58.227 54.223 22.669 1.00 31.60
              MOTA
                                                                                                                                                               6
                                                 PRO E 100
                             7362
                                        CB
              MOTA
                                                                                57.906 55.190 23.725 1.00 32.57
                                                                                                                                                               6
                                                                                                                                  1.00 35.44
                                        CG PRO E 100
              MOTA
                             7363
                                                                                                 51.719 22.769
                                                                                                                                                                6
                                                                                58.529
                                                  PRO E 100
                                        С
    55
                             7364
              MOTA
                                                                                                                                    1.00 35.44
                                                                                                  51.546 23.041
                                                                                59.713
                                                  PRO E 100
               MOTA
                             7365
                                         0
                                                                        57.844 50.868 22.029
58.514 49.701 21.516
57.551 48.532 21.476
57.398 47.921 22.845
56.194 47.037 22.948
                                                                                                  50.868
                                                                                                                                   1.00 37.12
                             7366 N
                                                  GLN E 101
               MOTA
                                                                                                 49.701 21.516 1.00 38.35
                              7367 CA GLN E 101
               MOTA
                                                                                                 48.532 21.476 1.00 39.07
                              7368 CB GLN E 101
               MOTA
                                                                                                                                    1.00 43.00
                                                   GLN E 101
                                          CG
    60
                              7369
               MOTA
                                                                                                                                  1.00 48.55
                              7370 CD GLN E 101
               MOTA
```

					-193				_
	MOTA	7371	OE1 GI	N E 101	56.055		22.194		8
	MOTA	7372	NE2 GI	N E 101	55.298		23.885		7 6
	MOTA	7373		N E 101	59.146			1.00 37.98	8
•	MOTA	7374	O GI	IN E 101	58.749			1.00 36.86	7
5	MOTA	7375	N L	EU E 102	60.153			1.00 39.66	6
_	ATOM	7376		EU E 102	· 60.936			1.00 38.89	6
	ATOM	7377		EU E 102	60.911			1.00 36.07	6
	MOTA	7378	CG L	EU E 102	59.545			1.00 36.30	6
	MOTA	7379	CD1 L	EU E 102	59.712			1.00 37.57	6
10	MOTA	7380	CD2 L	EU E 102	58.809			1.00 37.42 1.00 37.90	6
	ATOM	7381		EU E 102	62.374	50.791		1.00 37.30	8
	MOTA	7382	0 L	EU E 102	62.909	50.784	20.312	1.00 40.00	7
	MOTA	7383		LA E 103	62.995	50.408	18.102	1.00 37.30	6
	MOTA	7384	CA A	LA E 103	64.395	50.007	18.127	1.00 37.72	6
15	MOTA	7385		LA E 103	64.577	48.634	17.504 17.351	1.00 38.02	6
	ATOM	7386		LA E 103	65.193	51.039	16.666	1.00 38.29	8
	MOTA	7387		LA E 103	64.645	51.890	17.469	1.00 40.78	7
	MOTA	7388		RG E 104	66.500	50.969	16.770	1.00 44.75	6
	MOTA	7389	CA P	RG E 104	67.344	51.911	17.771	1.00 44.40	6
20	MOTA	7390	CB P	ARG E 104	68.258	52.612 53.873	17.771	1.00 45.66	6
	MOTA	7391		ARG E 104	68.873	54.956	16.983	1.00 43.79	6
	MOTA	7392	CD I	ARG E 104	67.868	56.118	16.456	1.00 46.54	7
	MOTA	7393	NE A	ARG E 104	68.570 68.008	57.289	16.175	1.00 46.54	6
	MOTA	7394	CZ Z	ARG E 104		57.493	16.365	1.00 47.66	7
25	MOTA	7395	NH1	ARG E 104	66.711 68.760	58.266	15.698	1.00 49.69	7
	MOTA	7396		ARG E 104	68.142	51.099	15.763	1.00 46.58	6
	MOTA	7397	_	ARG E 104	68.775		16,119	1.00 47.46	8
	MOTA	7398		ARG E 104	68.081		14.497	1.00 48.34	7
	MOTA	7399		VAL E 105 VAL E 105	68.808		13.475	1.00 49.67	6
30	MOTA	7400		VAL E 105	67.869		12.388	1.00 49.06	6
	MOTA	7401		VAL E 105	68.643		11.431	1.00 49.26	6
	MOTA	7402	_	VAL E 105	66.731		13.010	1.00 49.99	6
	MOTA	7403		VAL E 105	69.883		12.805	1.00 51.57	6
0.5	MOTA	7404		VAL E 105	69.606		12.272	1.00 49.78	8
35	MOTA	7405 7406		VAL E 106	71.109	000	12.834	1.00 53.67	7
	MOTA	7400		VAL E 106	72.265	5 51.738	12.232	1.00 55.11	6
	MOTA	7407		VAL E 106	73.53	7 51.409	13.009	1.00 54.77	6 6
	MOTA	7409		VAL E 106	74.66	52.300	12.539	1.00 55.46	6
40	MOTA MOTA	7410		VAL E 106	73.28		14.507	1.00 57.64	6
40	ATOM	7411		VAL E 106	72.42		10.795	1.00 55.88	8
	MOTA			VAL E 106	72.21		10.508	1.00 57.82 1.00 55.80	7
	ATOM			SER E 107	72.81				6
	MOTA		_	SER E 107	72.97				6
45				SER E 107	73.61				8
	ATOM			SER E 107	74.70			4	6
	MOTA		7 C	SER E 107	73.73				8
	ATOM			SER E 107	73.57				7
	ATOM		9 N	ASP E 108	74.55				6
50			0 CA	ASP E 108	75.32	48.847			6
_	ATOM		1 CB	ASP E 108	76.69				6
	ATOM		2 CG	ASP E 108	76.59				
	MOTA	1 742	3 OD1	ASP E 108	75.65				8
	MOTA	4 742	4 OD2	ASP E 108	77.47				6
55	TOTA 6	4 742	25 C	ASP E 108	74.6		·		
	IOTA	4 742	26 O	ASP E 108	75.23 73.33				
	ATO			GLY E 109			-	2 1.00 60.49	6
	ATO			GLY E 109				3 1.00 61.38	6
-	OTA			GLY E 109 GLY E 109				1 1.00 60.99	8 (
60									7
	ATO	м 743	31 N	GLU E 110	13.2	•			

	W O 01/30	931					101,2101,014	· .
				-194				
	> mo>/	7422 (1	A GLU E 110	73.283	46.899	13.787	1.00 61.54	6
		7432 C		74.432			1.00 64.16	6
		7433 CI		74.946		15.755	1.00 67.88	6
		7434 C		75.559		15.684	1.00 72.22	6
_	MOTA	7435 C		75.936	45.401	14.554	1.00 72.61	8
5	MOTA	-	E1 GLU E 110	75.676	45.165	16.758	1.00 70.57	8
	MOTA		E2 GLU E 110	71.948	47.368	14.347	1.00 60.20	6
	MOTA	7438 C			48.418	13.949	1.00 59.08	8
	MOTA	7439 O		71.421	46.581	15.266	1.00 57.63	7
	MOTA	7440 N		71.403		15.885	1.00 54.53	6
10	ATOM	7441 C	A VAL E 111	70.116	46.893		1.00 53.43	6
	MOTA		B VAL E 111	69.065	45.797	15.557	1.00 53.30	6
	MOTA	7443 C	G1 VAL E 111	67.728	46.159	16.178	1.00 52.07	6
	ATOM	7444 C	G2 VAL E 111	68.932	45.631	14.053	1.00 52.07	6
	MOTA	7445 C	VAL E 111	70.231	47.017	17.406	1.00 52.50	8
15	MOTA	7446 C	VAL E 111	70.846	46.170	18.066	1.00 52.11	7
	MOTA	7447 N	1 LEU E 112	69.641	48.070	17.961	1.00 50.09	6
	MOTA		CA LEU E 112	69.687	48.261	19.399	1.00 50.92	
	MOTA		CB LEU E 112	70.546	49.468	19.770	1.00 55.28	6
	MOTA		CG LEU E 112	71.820	49.846	18.992	1.00 58.58	6
20		7451	CD1 LEU E 112	72.649	48.603	18.629	1.00 59.41	6
20	ATOM	7452	CD2 LEU E 112	71.428	50.603	17.742	1.00 58.46	6
	MOTA		C LEU E 112	68.286	48.485	19.930	1.00 50.61	6
	ATOM		110	67.628	49.437	19.535	1.00 50.59	8
	MOTA		443	67.835	47.597	20.816	1.00 49.12	7
0.5	MOTA			66.514	47.690	21.420	1.00 46.39	6
25	MOTA		442	65.635	46.500	21.003	1.00 45.58	6
	MOTA			64.235	46.491	21.610	1.00 44.58	6
	MOTA		CG TYR E 113	63.453	47.650	21.655	1.00 45.06	6
	MOTA		CD1 TYR E 113	62.162	47.632	22.177	1.00 44.35	6
	MOTA		CE1 TYR E 113	63.684	45.318	22.105	1.00 43.68	6
30	ATOM		CD2 TYR E 113	62.395	45.287	22.629	1.00 45.23	6
	MOTA		CE2 TYR E 113		46.444	22.663	1.00 46.53	6
	MOTA	7463	CZ TYR E 113	61.633	46.399	23.183	1.00 46.01	8
	MOTA	7464	OH TYR E 113	60.346		22.915	1.00 46.41	6
	MOTA	7465	C TYR E 113	66.721		23.463	1.00 46.43	8
35	MOTA	7466	O TYR E 113	67.194	48.774	23.572	1.00 46.91	7
	ATOM	7467	N MET E 114	66.363		25.011	1.00 48.35	6
	MOTA	7468	CA MET E 114	66.539		25.315		6
	MOTA	7469	CB MET E 114	67.635		26.737		6
	MOTA	7470	CG MET E 114	68.053		27.017		16
40	MOTA	7471	SD MET E 114	68.981				6
	MOTA	7472	CE MET E 114	70.586				6
	MOTA	7473	C MET E 114	65.255				8
	ATOM	7474	O MET E 114	65.095				7
	MOTA	7475	N PRO E 115	64.325				6
45		7476	CD PRO E 115	64.34	L 46.978			6
40	MOTA	7477	CA PRO E 115	63.05		26.572		6
	MOTA	7478	CB PRO E 115	62.15				6
	MOTA	7479	CG PRO E 115	63.08			44	6
	MOTA	7480	C PRO E 115	63.18	48.685			8
50		7481	O PRO E 115	63.99	7 47.940			7
50	MOTA		N SER E 116	62.39	7 49.51			
			CA SER E 116	62.42	8 49.51	4 30.21		6
	MOTA		CB SER E 116	62.11				6
	MOTA			62.19		1 32.18	1 1.00 44.88	8
	MOTA		116	61.34				6
55			110	60.19		2 30.24	6 1.00 46.37	8
	MOTA			61.70		4 31.44		7
	MOTA		417	60.75			1 1.00 40.36	6
	ATOM		117	61.18	_		4 1.00 39.17	6
_	MOTA		CB ILE E 117	60.25		0 31.79		6
60				61.20		·		6
	MOTA	1 7492	CG1 ILE E 117	01.2				

	0 01,00							-	
					-195				
	ATOM	7493	CD1 T	LE E 117	61.883	43.985		1.00 35.74	6
	ATOM		C I	LE E 117	60.561	46.387		1.00 43.14	6
	ATOM		0 I	LE E 117	61.525	46.400		1.00 44.32	8
	MOTA			RG E 118	59.305	46.266		1.00 43.03	7
5	ATOM	7497		RG E 118	59.014	46.009		1.00 42.46	6
•	ATOM	7498		ARG E 118	57.907			1.00 40.98	6
	MOTA	7499		RG E 118	57.537	46.484	-	1.00 39.32	6
	MOTA	7500		ARG E 118	56.671		37.827	1.00 40.32	6
	ATOM	7501		ARG E 118	56.321		39.155	1.00 40.46	7
10	MOTA	7502		ARG E 118	55.762	47.717	40.108	1.00 38.25	6
10	ATOM	7502		ARG E 118	55.485	48.991	39.899	1.00 41.07	7
	ATOM	7504		ARG E 118	55.486		41.273	1.00 37.40	7
	ATOM	7505		ARG E 118	58.552	44.557	35.140	1.00 41.73	6
		7506		ARG E 118	57.738		34.309	1.00 41.59	8
15	MOTA	7507		GLN E 119	59.071		36.036	1.00 42.60	. 7
13	MOTA	7508		GLN E 119	58.718		36.016	1.00 43.62	· 6
	MOTA	7509		GLN E 119	59.460		34.842	1.00 41.24	6
	MOTA	7510		GLN E 119	59.220		34.624	1.00 40.90	6
	MOTA	7511		GLN E 119	59.795		33.304	1.00 40.75	6
20	MOTA	7512		GLN E 119	60.829		32.879	1.00 41.44	8
20	MOTA	7512	NE2	GLN E 119	59.12		32.654	1.00 44.30	7
	MOTA			GLN E 119	59.08		37.337	1.00 44.85	6
	MOTA	7514		GLN E 119	60.03		38.006	1.00 44.93	8
	MOTA	7515		ARG E 120	58.32		37.724	1.00 46.59	7
OF	MOTA	7516	N CA	ARG E 120	58.61		38.969	1.00 49.63	6
25	MOTA	7517 7518		ARG E 120	57.32			1.00 52.24	6
	MOTA			ARG E 120	56.51		40.037	1.00 59.37	6
	MOTA	7519	CD	ARG E 120	55.73		41.301	1.00 65.41	6
	MOTA	7520	NE	ARG E 120	56.51		42.518	1.00 68.76	7
00	MOTA	7521	CZ	ARG E 120	56.46			1.00 69.55	6
30	MOTA	7522		ARG E 120	55.68			1.00 67.60	7
	MOTA	7523	NULL	ARG E 120	57.15		44.702	1.00 69.98	7
	MOTA	7524		ARG E 120	59.36			1.00 48.95	6
	MOTA	7525	C	ARG E 120	59.18			1.00 47.74	8
0.5	MOTA	7526	0	PHE E 121	60.21			1.00 47.82	7
35	MOTA	7527	N	PHE E 121	60.99			1.00 46.24	6
	MOTA	7528	CA	PHE E 121	62.45			1.00 42.79	6
	MOTA	7529	CB	PHE E 121	62.62			1.00 43.16	6
	MOTA	7530	CG	PHE E 121	62.43			1.00 42.55	6
40	MOTA	7531	CDI		62.94		·	1.00 41.67	6
40	MOTA	7532		PHE E 121	62.5			1.00 44.29	6
	MOTA	7533		PHE E 121	63.0	<u>-</u>		1.00 39.85	6
	MOTA	7534		PHE E 121	62.8			1.00 43.74	6
	MOTA	7535		PHE E 121	60.9			1.00 46.96	6
4=	MOTA	7536			60.6			1.00 44.85	8
45	MOTA	7537		PHE E 121	61.3			1.00 50.04	7
	MOTA	7538		SER E 122	61.5			1.00 50.97	6
	MOTA	7539		SER E 122	60.8	_			6
	MOTA	7540		SER E 122	60.9			1.00 54.83	8
	MOTA			SER E 122	63.0				6
50				SER E 122	63.6				8
	MOTA			SER E 122	63.5				
	MOTA			CYS E 123	65.0				. 6
	MOTA			CYS E 123	65.3			1.00 58.47	6
	MOTA			CYS E 123	64.3				
55				CYS E 123	65.7			1.00 53.82	6
	MOTA			CYS E 123	65.2			11	16
	MOTA			CYS E 123	66.5			1.00 61.78	3 7
	MOTA			ASP E 124				7 1.00 63.06	5 6
	MOTA			ASP E 124	68.4			1.00 63.79	9 6
60				ASP E 124	68.6				
	MOTA	1 755	3 CG	ASP E 124	00.0	,,,			

PCT/EP01/01457

WO 01/58951

	W O 01/50	751							
					-196				
	MOTA	7554	001	ASP E 124	67.970	33.502		1.00 63.75	8
	MOTA	7555	002	ASP E 124	69.396	32.058	48.094	1.00 65.17	8
		7556	C .	ASP E 124	66.953	35.636		1.00 63.18	6
	MOTA	7557		ASP E 124	67.748			1.00 63.39	8
5	MOTA	7558		VAL E 125	66.031		47.936	1.00 63.67	7
3	MOTA			VAL E 125	65.869		48.586	1.00 63.68	6
	MOTA	7559		VAL E 125	64.370	37.506		1.00 61.88	6
	MOTA	7560			64.195	38.794		1.00 58.52	6
	MOTA	7561		VAL E 125	63.751			1.00 59.91	6
4.0	MOTA	7562		VAL E 125	66.501	37.157	49.987	1.00 64.88	6
10	MOTA	7563	_	VAL E 125		38.214	50.551	1.00 66.59	8
	MOTA	7564	_	VAL E 125	66.768	35.975	50.544	1.00 64.96	7
	MOTA	7565	N	SER E 126	66.745	35.870	51.874	1.00 64.47	6
	MOTA	7566	CA	SER E 126	67.335		52.185	1.00 62.82	6
	MOTA	7567	CB	SER E 126	67.672	34.410	51.267	1.00 61.35	8
15	MOTA	7568	OG	SER E 126	68.617	33.901	52.013	1.00 65.71	6
	MOTA	7569	С	SER E 126	68.588	36.729	51.165	1.00 65.59	8
	MOTA	7570	0	SER E 126	69.494	36.690		1.00 66.30	7
	MOTA	7571	N	GLY E 127	68.632	37.519	53.082	1.00 67.81	6
	MOTA	7572	CA	GLY E 127	69.788	38.369	53.309	1.00 69.06	6
20	MOTA	7573	C	GLY E 127	69.595	39.800	52.848	1.00 69.45	8
	MOTA	7574	0	GLY E 127	70.471	40.633	53.037	1.00 09.45	7
	MOTA	7575	N	VAL E 128	68.444	40.093	52.253	1.00 70.68	6
	ATOM	7576	CA	VAL E 128	68.179	41.438	51.771	1.00 72.21	6
	ATOM	7577	CB	VAL E 128	66.784	41.575	51.127	1.00 70.88	
25	MOTA	7578		VAL E 128	66.771	40.882	49.794	1.00 74.99	6
20	ATOM	7579	CG2	VAL E 128	65.722	40.993	52.039	1.00 69.09	6
	ATOM	7580	c	VAL E 128	68.233	42.480	52.855	1.00 73.85	6
	ATOM	7581	Ö	VAL E 128	68.855	43.525	52.678	1.00 74.59	8
		7582	N	ASP E 129	67.579	42.197	53.977	1.00 75.59	7
30	MOTA	7583	CA	ASP E 129	67.506	43.170	55.046	1.00 77.34	6
30	MOTA	7584	CB	ASP E 129	66.583	42.691	56.164	1.00 78.29	6
	MOTA	7585	CG	ASP E 129	65.952	43.864	56.939	1.00 80.26	6
	MOTA	7586		ASP E 129	64.733	43.805	57.257	1.00 82.07	8
	MOTA		ODI	ASP E 129	66.674	44.848	57.231	1.00 78.55	8
0.5	ATOM	7587	C	ASP E 129	68.825	43.625	55.628	1.00 78.37	6
35	MOTA	7588		ASP E 129	68.852	44.624	56.362	1.00 78.49	8
	MOTA	7589	0	THR E 130	69.925	42.942	55.302	1.00 79.16	7
	MOTA	7590		THR E 130	71.201	43.391	55.847	1.00 80.17	6
	MOTA	7591		THR E 130	71.162	43.351	57.393	1.00 83.36	6
	MOTA	7592	CB	THR E 130	70.028		57.803	1.00 84.91	8
40	MOTA	7593			71.096		57.995	1.00 82.87	6
	MOTA	7594			72.505		55.445	1.00 78.82	6
	MOTA	7595		THR E 130	72.549		55.068	1.00 78.45	8
	ATOM	7596		THR E 130	73.564		55.572	1.00 78.85	7
	ATOM	7597		GLU E 131	74.961		55.353	1.00 78.23	6
45	MOTA	7598		GLU E 131	75.292		56.187	1.00 80.76	6
	MOTA	7599		GLU E 131	75.507		57.686	1.00 82.62	6
	MOTA	7600		404			58.543	1.00 83.46	6
	MOTA			GLU E 131	75.241		58.186		8
	MOTA				75.740				. 8
50	MOTA	7603	3 OE		74.534				6
	MOTA	760	4 C	GLU E 131	75.434				8
	MOTA	760	5 0	GLU E 131	75.646				7
	MOTA	760	6 N	SER E 132	75.658				6
	MOTA		7 CA	SER E 132	76.10				6
55				SER E 132	76.77				8
	MOTA			SER E 132	75.89				6
	MOTA			SER E 132	74.85				8
	ATOM			SER E 132	74.92				
	ATOM			GLY E 133	73.71				6
60				4 GLY E 133	72.45				_
	ATOM			GLY E 133	72.12	7 40.179	50.631	L 1.00 67.70	U
	711.01								

	W O 01/36	931							101/2101/01	
						-197				
	ATOM	7615	O GI	Y E 13	3	72.686			1.00 67.31	8
				A E 13		71,205	40.256	49.681	1.00 66.03	7
	MOTA			A E 13		70.799	39.081	48.931	1.00 64.43	б
	ATOM			A E 13		69.275	38.990	48.879	1.00 64.83	6
=	MOTA			LA E 13		71.363	39.108	47.512	1.00 63.34	6
5	MOTA			LA E 13		71.825	40.148	47.014	1.00 61.70	8
	MOTA	7620				71.339	37.944	46.875	1.00 61.78	7
	MOTA	7621		HR E 13		71.813	37.817	45.515	1.00 61.48	6
	MOTA	7622		HR E 13 HR E 13		73.108	37.043	45.446	1.00 62.04	6
40	MOTA	7623				74.093	37.715	46.237	1.00 63.94	8
10	MOTA	7624	OGI T	HR E 13 HR E 13	5	73.590	36.970	44.012	1.00 63.05	6
	MOTA	7625				70.741	37.102	44.718	1.00 61.03	6
	MOTA	7626		HR E 13		70.522	35.886	44.839	1.00 59.53	8
	MOTA	7627		HR E 13		70.049	37.901	43.919	1.00 59.40	7
4-	MOTA	7628		YS E 13		68.975	37.422	43.083	1.00 57.62	6
15	MOTA	7629		YS E 13		69.530	37.254	41.669	1.00 56.65	6
	MOTA	7630		YS E 13		69.990	38.220	41.054	1.00 54.61	8
	MOTA	7631	0 0	YS E 13	36		38.442	43.129	1.00 55.65	6
	MOTA	7632		YS E 13		67.843	38.178	41.946	1.00 55.99	16
	MOTA	7633		YS E 13		66.510	36.016	41.180	1.00 56.36	7
20	MOTA	7634		RG E 1		69.517	35.717	39.853	1.00 57.23	6
	MOTA	7635		RG E 1		70.025	34.437	39.871	1.00 58.80	6
	MOTA	7636		RG E 1		70.861	34.513	40.774	1.00 62.70	6
	MOTA	7637		RG E 1		72.068	33.125	41.241	1.00 66.89	6
	MOTA	7638		ARG E 1		72.482	33.123	42.500	1.00 70.82	7
25	MOTA	7639		ARG E 1		73.230	33.659	42.633	1.00 71.90	6
	MOTA	7640		ARG E 1		74.469	34.130	41.578	1.00 70.38	7
	MOTA	7641		ARG E 1		75.134	33.674	43.832	1.00 71.22	7
	MOTA	7642	NH2	ARG E 1	.37	75.042	35.545	38.894	1.00 56.91	6
	MOTA	7643		ARG E 1		68.863	34.822	39.177	1.00 56.92	8
30	MOTA	7644	-	ARG E 1		67.909	36.215	37.754	1.00 54.63	7
	MOTA	7645		ILE E 1		68.970	36.215	36.716	1.00 51.98	6
	MOTA	7646		ILE E 1		67.966	37.587	36.468	1.00 51.76	6
	ATOM	7647		ILE E 1		67.432 66.432	37.573	35.333	1.00 49.89	6
	MOTA	7648		ILE E 1			38.137	37.757	1.00 50.16	6
35	MOTA	7649		ILE E 1		66.817 66.476	39.606	37.681	1.00 47.06	6
	MOTA	7650		ILE E 1		68.611	35.655	35.434	1.00 52.26	6
	MOTA	7651		ILE E		69.557	36.261	34.933	1.00 52.12	8
	MOTA	7652		ILE E		68.105	34.542	34.901	1.00 52.70	7
	MOTA	7653		LYS E		68.656	33.961	33.667	1.00 53.32	6
40	MOTA	7654		LYS E		68.877	32.455	33.822	1.00 53.63	6
	MOTA	7655		LYS E		69.732	32.075	35.013	1.00 57.59	6
	MOTA	7656	CG	LYS E	139	70.150		34.967	1.00.59.76	6
	MOTA	7657		LYS E	139	71.183		33.869		6
	MOTA	7658		LYS E	139	71.163		33.787		7
45	MOTA	7659		LYS E	139	67.738				6
	MOTA	7660	·C	LYS E	139					8
	MOTA	7661		LYS E	139	66.572				7
	MOTA	7662		ILE E		68.264				6
	MOTA	7663		ILE E		67.449				6
50	MOTA	7664		ILE E	140	66.995				
	MOTA	7665	CG2	ILE E	140	66.543				6
	MOTA	7666	GCG1	ILE E		68.136				
	MOTA	7667	CD1	ILE E	140	67.815				
	MOTA			ILE E		68.145				
55	MOTA			ILE E		69.295				
	MOTA	7670	ИС	GLY E	141	67.434				6
	MOTA	767	1 CA	GLY E		67.98		_		6
	MOTA			GLY E		66.88				
	MOTA			GLY E		65.70				7
60) ATOM			SER E	142	67.24				
	ATOM	1 767	5 CA	SER E	142	66.24	T 35.31,	± 2J.JJ.		_

•	WO 01/5 8 9	51				100			PCT/EP01/0145	7
	MOTA	7676	СВ	SER E	142	-198 66.883	32.177	22.214	1.00 44.37	6
	MOTA	7677		SER E		65.913	31.657	21.329	1.00 40.29	8
	MOTA	7678	С	SER E		65.386	31.346	23.997	1.00 47.72	6
	MOTA	7679	0	SER E	142	65.880	30.376	24.584	1.00 48.09	8
5	MOTA	7680	N.	TRP E	143	64.097	31.439	23.701	1.00 47.51	7
	MOTA	7681		TRP E		63.165	30.406	24.101	1.00 46.17	6
	MOTA	7682		TRP E		61.780	31.025	24.327	1.00 45.01	6
	MOTA	7683		TRP E		60.808	30.096	24.968	1.00 42.92	6
10	MOTA	7684		TRP E		60.799	29.697	26.337	1.00 41.62	6
10	MOTA	7685		TRP E		59.721	28.803	26.505 27.442	1.00 39.45 1.00 42.26	6 6
	MOTA	7686 7687		TRP E		61.601 59.764	30.008 29.448	24.371	1.00 42.20	6
	ATOM ATOM	7688		TRP E		59.106	28.669	25.288	1.00 41.08	7
	ATOM	7689		TRP E		59.423	28.216	27.736	1.00 39.02	6
15	ATOM	7690		TRP E		61.305	29.426	28.662	1.00 40.87	6
	MOTA	7691		TRP E		60.223	28.540	28.799	1.00 41.01	6
	MOTA	7692	С	TRP E	143	63.067	29.281	23.097	1.00 46.14	6
	MOTA	7693	0	TRP E	143	62.816	28.147	23.467	1.00 47.72	8
	MOTA	7694	N	THR E		63.277	29.579	21.821	1.00 46.28	7
20	MOTA	7695	CA	THR E		63.141	28.539	20.808	1.00 44.88	6
	MOTA	7696	CB	THR E		61.961	28.863	19.859	1.00 42.99	6
	MOTA	7697		THR E		62.131	30.174	19.308	1.00 42.03	8
	MOTA	7698		THR E		60.655	28.824	20.609	1.00 40.32 1.00 46.55	6 6
25	MOTA	7699	C	THR E		64.378 64.434	28.276 27.294	19.969 19.243	1.00 46.91	8
25	MOTA MOTA	7700 7701	N O	HIS E		65.367	29.151	20.060	1.00 48.37	7
	ATOM	7702	CA	HIS E		66.576	28.973	19.275	1.00 50.06	6
	MOTA	7703	CB	HIS E		66.937	30.265	18.541	1.00 49.35	6
	MOTA	7704	CG	HIS E		65.947	30,669	17.492	1.00 49.26	6
30	MOTA	7705		HIS E		65.676	30.143	16.275	1.00 49.17	6
	MOTA	7706		HIS E		65.112	31.756	17.634	1.00 47.03	7
•	MOTA	7707	CE1	HIS E	145	64.371	31.883	16.548	1.00 48.38	6
	MOTA	7708	NE2	HIS E	145	64.694	30.917	15.708	1.00 50.40	7
	MOTA	7709	C	HIS E		67.754	28.529	20.125	1.00 51.77	6
35	MOTA	7710	Ο.	HIS E		68.096	29.153	21.129	1.00 50.03	8 7
	MOTA	7711	N	HIS E		68.371	27.427	19.710	1.00 55.46 1.00 57.69	6
	MOTA	7712	CA	HIS E		69.530	26.886 25.377	20.418 20.162	1.00 57.05	6
	MOTA	7713	CB	HIS E		69.654 69.679	25.377	18.715	1.00 56.24	6
40	MOTA	7714 7715	CD3	HIS E		70.477	25.442	17.707	1.00 55.97	6
40	ATOM ATOM	7716		HIS E		68.798	24.121	18.157	1.00 58.10	7
	ATOM	7717		HIS E		69.053	24.005	16.863	1.00 58.23	6
	ATOM	7718	NE2	HIS E	146	70.068	24.797	16.566	1.00 57.28	7
	ATOM	7719	C	HIS E		70.801	27.612	19.971		6
45	ATOM	7720	0	HIS E		70.775	28.455	19.064	1.00 59.37	8
	MOTA	7721	N	SER E	147	71.908	27.269	20.618	1.00 60.00	7
	MOTA	7722	CA	SER E		73.218	27.872	20.356	1.00 60.54	6
	MOTA	7723	CB	SER E		74.268	27.134	21.185	1.00 60.36	6
	MOTA	7724	OG	SER E		74.082	25.728	21.071	1.00 61.90 1.00 60.61	8 6
50	MOTA	7725	C	SER E		73.690	27.960	18.897	1.00 60.32	8
	MOTA	7726	0	SER E		74.491 73.197	28.837 27.072	18.553 18.041	1.00 59.60	7
	MOTA	7727	N	ARG E		73.611	27.072	16.646	1.00 60.89	6
	MOTA	7728 7729	CA CB	ARG E		73.307	25.722	15.996	1.00 66.00	6
55	MOTA	7730		ARG E	_	73.902	24.527	16.756	1.00 74.00	é
JJ	MOTA MOTA	7731	CG CD	ARG E		73.462	23.177	16.169	1.00 79.80	6
	ATOM	7732	NE	ARG E		73.749	22.052	17.077	1.00 85.45	7
	MOTA	7733	CZ	ARG E		74.973	21.680	17.475	1.00 86.76	6
	ATOM	7734		ARG E		76.045	22.338	17.046	1.00 87.13	7
60	MOTA	7735		ARG E		75.130	20.650	18.306	1.00 86.87	7
J.	MOTA	7736	С	ARG E		72.942	28.189	15.847	1.00 59.62	6

- -· =

.

•	WO 01/589	951										PCT/I	E P 01/01	157
	* =0.1	9929	_	. D	1 4 0		199	-	8.564	14 7	66	1 00	58.11	8
	ATOM	7737		ARG E : GLU E			.418		28.707	14.7 16.3			58.68	7
	MOTA	7738 7739		GLU E			067		9.756	15.7			56.72	· 6
	ATOM ATOM	7740		GLU E			.598		9.337	15.6			55.99	6
5	ATOM	7741		GLU E		_	.435		7.854	15.3			57.25	6
U	ATOM	7742		GLU E			1.992		7.402	15.2			57.65	6
	ATOM	7743		GLU E			1.166		27.825	16.0		1.00	58.97	8
	ATOM	7744		GLU E		67	7.684	2	26.606	14.3	32	1.00	56.32	8
	MOTA	7745	С	GLU E	149	7:	L.214	3	31.073	16.4	163	1.00	55.95	6
10	MOTA	7746	0	GLU E	149	7:	1.423	3	32.122	15.8			54.41	8
	MOTA	7747	N	ILE E	150	7:	1.109	3	31.012	17.7			55.27	7
	ATOM	7748	CA	ILE E			1.265		32.202	18.6			54.72	6
	MOTA	7749	CB	ILE E			9.922		32.686	19.2			54.60	6
	MOTA	7750		ILE E			0.190		33.711	20.3			51.29	6 6
15	MOTA	7751		ILE E			9.051		33.354	18.3			53.90 52.06	6
	MOTA	7752		ILE E			7.738		33.855	18.7 19.7			55.47	6
	ATOM	7753	C	ILE E			2.238 2.226		31 <i>.</i> 954 30.898	20.3			54.39	8
	MOTA	7754	0	SER E			2.220 3.083		32.948	19.9			56.26	7
20	MOTA MOTA	7755 7756	N CA	SER E			4.055		32.898	21.0			59.09	6
20	ATOM	7757	CB	SER E			5.478		32.752	20.4			59.25	6
	ATOM	7758	OG	SER E			5.826		33.853	19.6		1.00	59.55	8
	MOTA	7759	C	SER E			3.904		34.226	21.			59.98	6
	MOTA	7760	ō	SER E			3.793		35.283	21.	139	1.00	59.94	8
25	MOTA	7761	N	VAL E	152	7	3.878	}	34.172	23.	096		60.88	7
	ATOM	7762	CA	VAL E		7	3.739		35.380	23.			62.73	6
	MOTA	.7763	CB	VAL E			2.628		35.233	24.			61.31	6
	MOTA	7764		VAL E			1.339		34.777	24.			58.78	6
	MOTA	7765		VAL E			3.067		34.241	26.			62.59 64.27	6 6
30	MOTA	7766	C	VAL E			5.054		35.633	24. 24.			63.76	8
	ATOM	7767	0	VAL E			5.743		34.687 36.904	24.			66.67	7
	MOTA	7768	N	ASP E			5.393 6.650		37.261	25.			70.32	6
	MOTA	7769	CA	ASP E			7.713		37.471	24.			70.77	6
25	MOTA	7770	CB CG	ASP E			7.832		36.272	23.			74.19	6
35	MOTA MOTA	7771 7772		ASP E			8.483		35.261	23.		1.00	75.87	8
	ATOM	7773		ASP E			7.265		36.331		319	1.00	73.45	8
	ATOM	7774	C	ASP E			6.531		38.533	26.	304		72.18	
	ATOM	7775	Ö	ASP E		7	5.835	5	39.481	25.	922		72.90	
40	MOTA	7776	N	PRO E		7	7.187	7	38.561	27.	478		73.33	
	MOTA	7777	CD	PRO E	154		7.671		37.398		243		72.54	
	MOTA	7778	CA	PRO E			7.123		39.755		332		75.06	
	ATOM	7779	CB	PRO E			7.749		39.279		642		74.00	
	MOTA	7780	CG	PRO E					37.823		676		74.05 77.63	_
45	MOTA	7781	С	PRO E			77.91		40.901		688		78.05	
	MOTA	7782	0	PRO E			78.50		40.717 42.066		338	1 00	81.26	7
	MOTA	7783	N	THR E			77.940 78.63		43.230		781	1.00	85.03	6
	ATOM	7784	CA	THR E			77.62		44.147		020		83.83	
50	MOTA	7785	CB OC1	THR E			76.71		44.749		956	1.00	81.33	8
30	MOTA MOTA	7786 7787	CG2				76.81		43.341		020		83.47	
	MOTA	7788	C	THR E			79.41		44.101		803		88.40) 6
	ATOM	7789	Ö	THR E			79.90		43.592	29.	825	1.00	88.82	8
	ATOM	7790		THR E		•	79.52	7	45.405	28.	487		91.48	
55	MOTA	7791	CA	THR E	156		80.20		46.443		. 288		93.5	
-	ATOM	7792		THR E			79.61		47.854		.002		93.3	
	MOTA	7793		L THR E			79.69		48.136		. 596		92.73	
	MOTA	7794		2 THR E			80.37		48.925		.813		92.2	
	MOTA	7795		THR E			80.16		46.249		.803 476		95.69 95.9	
60	MOTA	7796		THR E			79.17		46.584		.476 .340		97.8	
	MOTA	7797	N	GLU E	T2/		81.26	4	45.733	2.7	40	1.0	, ,,,,,,	. ,

PCT/EP01/01457

						-200				
	MOTA	7798	CA	GLU E 157		81.365	45.481	32.776	1.00100.21	6
	MOTA	7799	CB	GLU E 157		82.361	44.343	33.018	1.00101.17	6
	ATOM	7800		GLU E 157		82.198	43.190	32.046	1.00103.80	6
	MOTA	7801		GLU E 157		83.222	42.107	32.296	1.00105.78	6
5	ATOM	7802		GLU E 157		84.423	42.466	32.375	1.00105.64	8
J	ATOM	7802		GLU E 157		82.828	40.907	32.410	1.00107.35	8
			C	GLU E 157		81.817	46.729	33.550	1.00100.48	6
	ATOM	7804	0	GLU E 157		81.869	46.719	34.798	1.00100.82	8
	ATOM	7805		ASN E 158		82.151	47.793	32.818	1.00 99.54	7
40	MOTA	7806	N			82.620	49.011	33,461	1.00 98.41	6
10	MOTA	7807	CA	ASN E 158		83.235	49.953	32.426	1.00100.23	6
	MOTA	7808	CB	ASN E 158			49.283	31,604	1.00101.57	6
	MOTA	7809	CG	ASN E 158		84.338	48.768	32.152	1.00100.21	8
	MOTA	7810		ASN E 158		85.334	49.286	30.274	1.00102.69	7
	MOTA	7811		ASN E 158		84.165		34.156	1.00 96.86	6
15	MOTA	7812	С	ASN E 158		81.456	49.701		1.00 96.41	8
	MOTA	7813	0	ASN E 158		81.185	49.443	35.341	1.00 94.72	7
	MOTA	7814	N	SER E 159		80.791	50.578	33.395	1.00 94.72	6
•	ATOM	7815	CA	SER E 159		79.624	51.349	33.834		6
	MOTA	7816	CB	SER E 159		78.465	51.087	32.858	1.00 91.87	
20	MOTA	7817	OG	SER E 159		78.391	49.705	32.499	1.00 92.44	8
	MOTA	7818	С	SER E 159		79.169	51.080	35.269	1.00 88.56	6
	ATOM	7819	0	SER E 159		78.823	49.947	35.614	1.00 89.22	8
	MOTA	7820	N	ASP E 160		79.171	52.119	36.102	1.00 85.19	7
	MOTA	7821	CA	ASP E 160		78.744	51.966	37.495	1.00 81.21	6
25	MOTA	7822	CB	ASP E 160		78.527	53.327	38.157	1.00 80.51	6
20	ATOM	7823	CG	ASP E 160		78.005	53.194	39.574	1.00 79.98	6
	ATOM	7824		ASP E 160		77.424	54,174	40.079	1.00 80.37	8
	MOTA	7825		ASP E 160		78.184	52.104	40.178	1.00 78.39	8
		7826	C	ASP E 160		77.426	51.202	37.525	1.00 78.59	6
30	MOTA MOTA	7827	Ö	ASP E 160		76.427	51.669	36.959	1.00 77.98	8
30		7828	N	ASP E 161		77.427	50.043	38.185	1.00 75.05	7
	MOTA		CA	ASP E 161		76.233	49.203	38.283	1.00 71.67	6
	MOTA	7829		ASP E 161		76.473	48.017	39.226	1.00 70.39	6
	MOTA	7830	CB	ASP E 161		77.428	46.994	38.641	1.00 70.69	б
0-	MOTA	7831	CG	ASP E 161		77.389	46.782	37.416	1.00 70.97	8
35	MOTA	7832		ASP E 161		78.211	46.386	39.400	1.00 71.91	8
	ATOM	7833		ASP E 161		74.968	49.931	38.732	1.00 70.49	6
	MOTA	7834	С	ASP E 161		73.864	49.439	38.514	1.00 71.58	8
	MOTA	7835	0			75.099	51.093	39.356	1.00 68.11	7
4.0	MOTA	7836	N	SER E 162		73.903	51.792	39.785	1.00 66.58	6
40	MOTA	7837	CA	SER E 162		73.771	51.731	41.308	1.00 66.49	6
	MOTA	7838	CB	SER E 162		74.786	52.478	41.938	1.00 64.63	8
	MOTA	7839	oG	SER E 162		73.856	53.237	39.319	1.00 65.96	6
	MOTA	7840	_	SER E 162		73.250	54.088	39.972	1.00 64.77	8
	MOTA	7841		SER E 162			53.514	38.178	1.00 65.61	7
45	MOTA	7842		GLU E 163		74.475	54.872	37.676	1.00 67.53	· 6
	MOTA	7843		GLU E 163		74.474		36.631	1.00 70.35	6
	MOTA	7844				75.582	55.051	35.213	1.00 72.94	6
	MOTA	7845	CG			75.237	54.661	34.225	1.00 76.12	6
	MOTA	7846	CD	GLU E 163		76.338			1.00 77.12	8
50	MOTA	7847	OE			77.424		34.241	1.00 76.02	8
	MOTA	7848	OE			76.118			1.00 76.02	6
	MOTA	7849	C	GLU E 163		73.108				8
	ATOM	7850		GLU E 163	}	72.873				7
	MOTA	7851	N	TYR E 164	Ł	72.211				
55	MOTA	7852				70.848				6
	ATOM	7853		3 TYR E 164		70.555				6
	ATOM		1 CG	TYR E 164		71.386				6
	ATOM		5 CI	1 TYR E 164	1	72.237				6
	MOTA		5 CE	E1 TYR E 16	1	73.040		32.351		6
60				2 TYR E 16	4	71.350				6
	MOTA			E2 TYR E 16		72.154	55.805	32.471	1.00 67.79	6

-200

,	WO 01/589	951			-201				PCT	EP01/014	57
	ATOM	7859	CZ S	TYR E 164	72.99	4 54	.867	31.867	1.00	67.33	6
	ATOM	7860		TYR E 164	73.74		.230	30.765	1.00		8
	ATOM	7861		TYR E 164	69.83		.174	37.574	1.00		6
	ATOM	7862	-	TYR E 164	68.64		.458	37.442	1.00		8
5	MOTA	7863	_	PHE E 165	70.30	9 53	.552	38.646	1.00		7
-	ATOM	7864		PHE E 165	69.42		.139	39.717		59.92	6
	MOTA	7865		PHE E 165	70.20		.378	40.776		58.36	6
	ATOM	7866		PHE E 165	69.34		515	41.645		58.01	6
	MOTA	7867		PHE E 165	68.67		.427	41.110		55.31 58.36	6 6
10	MOTA	7868		PHE E 165	69.18		. 802	42.994		56.74	6
	MOTA	7869		PHE E 165	67.85		0.642 L.016	41.904 43.804		57.34	6
	MOTA	7870		PHE E 165	68.36		9.939	43.260		57.55	6
	MOTA	7871		PHE E 165 PHE E 165	67.70 68.73		1.324	40.356		60.15	6
4 =	MOTA	7872		PHE E 165	69.32		5.390	40.504		62.59	8
15	MOTA	7873		SER E 166	67.4		1.148	40.718		59.42	7
	MOTA	7874 7875	N CA	SER E 166	66.72		5.222	41.357	1.00	57.86	6
	ATOM ATOM	7876	CB	SER E 166	65.2		4.869	41.503	1.00	56.65	6
	MOTA	7877	OG	SER E 166	64.5		5.951	42.064		53.76	8
20	MOTA	7878	Č	SER E 166	67.3	25 5	5.425	42.733		56.88	6
	ATOM	7879	Ō	SER E 166	67.7	12 5	4.472	43.407		55.76	8
	MOTA	7880	N	GLN E 167	67.4		6.677	43.142		56.96	7 6
	MOTA	7881	CA	GLN E 167	67.9	-	7.010	44.443		58.28	6
	ATOM	7882	CB	GLN E 167	68.5		8.423	44,401		60.41 64.41	6
25	MOTA	7883	CG	GLN E 167	67.5		9.465	43.941 43.599	1.00	66.50	6
	MOTA	7884	CD	GLN E 167	68.1		0.780 1.433	44.458		67.54	8
	MOTA	7885	OE1		68.7		1.184	42.330		68.48	7
	MOTA	7886	NE2	GLN E 167	68.0 66.8		6.924	45.532		57.21	6
00	MOTA	7887	С	GLN E 167 GLN E 167	67.1		6.835	46.720		56.91	8
30	MOTA	7888	0	TYR E 168	65.6		6.932	45.133		54.47	7
	MOTA	7889 7890	N CA	TYR E 168	64.5		6.877	46.111		53.18	6
	MOTA MOTA	7891	CB	TYR E 168	63.3	_	7.760	45.649		53.95	6
	ATOM	7892	CG	TYR E 168	63.8	81 5	9.125	45.249		53.27	6
35	ATOM	7893	CD1		64.1	.02 5	9.439	43.913		54.37	6
	ATOM	7894	CE1		64.6		0.672	43.541	1.00	56.01	6 6
	MOTA	7895	CD2		64.1		0.077	46.208	1.00	52.09	6
	MOTA	7896	CE2		64.7		51.304	45.856	1.00	57.20	6
	MOTA	7897	CZ	TYR E 168	64.9		51.599	44.522 44.177		59.36	8
40	MOTA	7898	OH	TYR E 168	65.4		52.815 55.470	46.431	1.00	52.65	6
	MOTA	7899	С	TYR E 168	64.0		55.282	47.189	1.00	53.48	8
	MOTA	7900	0	TYR E 168	63.1 64.7		54.479	45.861	1.00	51.93	7
	MOTA	7901	N	SER E 169	64.3	-	53.093			53.34	б
4 -	MOTA	7902	CA	SER E 169 SER E 169	65.		52.167	45.201	1.00	53.89	6
45	MOTA	7903		SER E 169	64.		50.807	45.514	1.00	50.40	8
	MOTA	7904 7905		SER E 169	64.		52.726	47.567		54.98	6
	MOTA MOTA	7906		SER E 169	65.		53.225	48.162		0 54.67	8
	MOTA	7907		ARG E 170	63.	875	51.844	48.131		0 56.35	7
50	MOTA	7908		ARG E 170	64.		51.404			0 56.22	6
-	ATOM	7909		ARG E 170	62.		50.568			0 57.55	6
	MOTA	7910		ARG E 170	61.		51.361			0 59.10 0 63.93	6 6
	ATOM	7911	. CD	ARG E 170	60.		50.785			0 67.80	
	MOTA	7912		ARG E 170	60.		49.382		_	0 68.39	
55		7913		ARG E 170			48.405 48.664		_	0 66.05	
	MOTA	7914		1 ARG E 170		577 784	47.163			0 71.45	
	MOTA	7915				342	50.563			0 56.43	
	MOTA			ARG E 170 ARG E 170		878	50.334		5 1.0	0 57.41	. 8
60	MOTA			PHE E 171		833	50.115	_	3 1.0	0 54.16	7
60						011	49.265			0 53.05	6
	MOTA	(24.	, ca		-						

•	WO 01/589	951					-202			PCT/EP01/014	57
		7000	an	DUT E	171	6	-202 6.665	47.926	47.747	1.00 51.94	6
	MOTA	7920 7921		PHE E			5.392	47.326	48.259	1.00 52.21	6
	MOTA MOTA	7921		PHE E			4.157	47.848	47.876	1.00 54.72	6
		7923		PHE E			5.416	46.288	49.180	1.00 52.12	6
5	MOTA	7923		PHE E			2.963	47.346	48.412	1.00 54.00	6
5	MOTA	7925		PHE E			4.233	45.781	49.719	1.00 52.15	6
	ATOM ATOM	7926	CZ	PHE E			3.008	46.313	49.334	1.00 53.26	6
	MOTA	7927	C	PHE E			8.181	49.909	47.698	1.00 54.03	6
	ATOM	7928	0	PHE E			8.056	50.993	47.137	1.00 55.23	8
10	ATOM	7929	N	GLU E			9.328	49.245	47.749	1.00 55.00	7
10	ATOM	7930	CA	GLU E			70.520	49.755	47.106	1.00 56.51	6
	ATOM	7931	CB	GLU E			71.385	50.513	48.120	1.00 58.70	6
	ATOM	7932	CG	GLU E			71.906	49.691	49.299	1.00 63.76	6
	ATOM	7933	CD	GLU E			72.716	50.527	50.300	1.00 66.16	б
15	MOTA	7934		GLU E			73.450	51.439	49.861	1.00 67.90	8
.0	ATOM	7935	OE2	GLU E			72.635	50.266	51.526	1.00 67.48	8
	ATOM	7936	C	GLU E		•	71.288	48.596	46.490	1.00 57.61	6
	ATOM	7937	ō	GLU E		•	71.161	47.451	46.917	1.00 57.07	8
	ATOM	7938	N	ILE E			72.077	48.891	45.470	1.00 58.83	7
20	MOTA	7939	CA	ILE E			72.844	47.850	44.802	1.00 60.44	6
	MOTA	7940	CB	ILE E			72.863	48.063	43.274	1.00 60.05	6
	ATOM	7941	CG2	ILE E			73.751	47.016	42.617	1.00 60.65	6
	MOTA	7942	CG1	ILE E			71.439	47.999	42.722	1.00 60.27	6
	ATOM	7943	CD1	ILE E			71.357	48.283	41.245	1.00 60.88	6
25	MOTA	7944	С	ILE E	173		74.289	47.760	45.275	1.00 60.89	6
	MOTA	7945	0	ILE E	173		75.011	48.752	45.342	1.00 60.64	8
	MOTA	7946	N	LEU E	174		74.715	46.555	45.595	1.00 62.24	7
	MOTA	7947	CA	LEU E	174		76.079	46.360	46.019	1.00 63.64	6
	MOTA	7948	СВ	LEU E			76.152	45.176	46.968	1.00 62.78	6
30	MOTA	7949	CG	LEU E			75.126	45.262	48.086	1.00 63.68	6 6
	MOTA	7950		LEU I			75.212	44.013	48.952	1.00 63.39	6
	ATOM	7951	CD2	LEU F			75.367	46.538	48.896	1.00 62.58 1.00 65.84	6
	MOTA	7952	С		E 174		76.908	46.093	44.760	1.00 65.84	8
	MOTA	7953	0		E 174		77.891	46.787	44.480	1.00 67.17	7
35	MOTA	7954	N		≅ 175		76.494	45.102	43.979	1.00 67.20	6
	MOTA	7955	CA		₹ 175		77.227	44.772	42.763	1.00 68.39	6
	MOTA	7956	СВ	ASP 3			78.496	43.999	43.148 41.961	1.00 67.83	6
	MOTA	7957	CG		E 175		79.385	43.673	41.192		8
	MOTA	7958	OD1	ASP	E 175		79.754	44.600	41.192	1.00 67.72	8
40	MOTA	7959		ASP	E 175		79.727	42.477 43.960	41.803	1.00 67.16	6
	MOTA	7960			E 175		76.358	43.300	42.216	1.00 66.38	8
	MOTA	7961		ASP			75.405	44.044	40.520	1.00 66.77	7
	MOTA	7962			E 176		76.692	43.329			6
	MOTA	7963			E 176		75.974 75.077	44.283	38.643		6
45	MOTA	7964	CB		E 176		74.430	43.524			6
	MOTA	7965	CG.	L VAL	E 176		74.009	44.902	39.537		6
	MOTA	7966		LAV S	E 1/0		76.979				6
	MOTA	7967			E 176		77.894				8
	MOTA	7968		VAL	E 176		76.796				7
50	MOTA	7969			E 177		77.682				6
	MOTA	7970			E 177 E 177		78.677		_		6
	MOTA	7971	. CB				77.962				8
	MOTA	7972		1 THR	E 177		79.630				6
	MOTA	7973			E 177 E 177		76.870				6
55		7974					75.849		_		8
	MOTA	7975			E 177 E 178		77.327				7
	MOTA	7976			E 178		76.642		_		6
	MOTA				E 178		76.151			1.00 75.43	6
60	MOTA				E 178		75.865				6
OU		_			E 178		74.935				6
	MOTA	, 50	. CL								

,	WO 01/58	951							PCT/EP01/014	57
						-203				
	MOTA	7981	OE1	GLN E	178	75.139	41.862	31.236	1.00 82.06	8
	MOTA	7982		GLN E		73.909	42.565	33.002	1.00 78.21	7
	MOTA	7983		GLN E		77.608	37.840	33.610	1.00 74.50	6
_	MOTA	7984		GLN E		78.661	38.205	33.086	1.00 74.89	8
5	MOTA	7985		LYS E		77.248	36.563	33.703	1.00 75.28	7
	MOTA	7986		LYS E		78.107	35.482	33.209	1.00 75.34	6 6
	MOTA	7987	СВ	LYS E		78.666	34.692	34.391	1.00 77.30 1.00 81.23	6
	MOTA	7988	CG	LYS E		79.186	35.600	35.515	1.00 81.23	6
40	MOTA	7989	CD	LYS E		79.593	34.805	36.763 37.981	1.00 83.73	6
10	MOTA	7990	CE	LYS E		79.779 78.496	35.727 36.431	38.332	1.00 82.75	7
	MOTA	7991	NZ	LYS E		77.274	34.554	32.353	1.00 74.24	6
	MOTA	7992	С	LYS E		76.409	33.850	32.882	1.00 74.20	8
	MOTA	7993	0	LYS E		77.528	34.533	31.045	1.00 72.18	7
15	MOTA	7994 7995	N CA	LYS E		76.747	33.674	30.155	1.00 70.93	6
13	ATOM ATOM	7996	CB	LYS E		77.062	34.017	28.694	1.00 71.21	6
	MOTA	7997	CG	LYS E		78.412	33.558	28.187	1.00 67.95	6
	ATOM	7998	CD	LYS E		78.327	32.136	27.630	1.00 67.85	6
	ATOM	7999	CE	LYS E		77.429	32.041	26.394	1.00 66.39	6
20	MOTA	8000	NZ	LYS E		78.005	32.722	25.197	1.00 67.24	7
	MOTA	8001	C	LYS E		77.014	32.199	30.429	1.00 69.92	б
	MOTA	8002	0		180	77.803	31.876	31.303	1.00 70.33	8
	MOTA	8003	N	ASN E	181	76.335	31,310	29.711	1.00 69.75	7
	MOTA	8004	CA	ASN E	181	76.570	29.881	29.878	1.00 70.27	6
25	MOTA	8005	CB	ASN E		76.563	29.495	31.362	1.00 69.84	6
	MOTA	8006	CG	ASN E		75.395	30.060	32.112	1.00 70.39	6
	MOTA	8007	OD1	ASN E		74.255	30.006	31.648	1.00 75.03 1.00 70.26	8 7
	ATOM	8008	ND2	ASN E		75.659	30.587	33.299	1.00 70.28	6
	MOTA	8009	С	ASN E		75.658	28.932	29.097 29.276	1.00 72.53	8
30	MOTA	8010	0	ASN E		74.438	28.918 28.121	28.236	1.00 72.33	7
	MOTA	8011	N	SER E		76.266 75.518	27.161	27.427	1.00 73.38	6
	MOTA	8012	CA	SER E		76.437	26.566	26.343	1.00 74.44	6
	MOTA	8013	CB	SER E		75.712	25.791	25.388	1.00 77.56	8
OF	MOTA	8014	OG	SER E		74.984	26.054	28.345	1.00 73.19	6
35	MOTA	8015	C O	SER E		75.527	25.836	29.428	1.00 73.57	8
	MOTA	8016 8017	N	VAL E		73.936	25.350	27.914	1.00 72.44	7
	MOTA MOTA	8018	CA	VAL E		73.341	24.295	28.738	1.00 71.01	6
	MOTA	8019	СВ	VAL E		72.582	24.906	29.956	1.00 69.59	6
40	ATOM	8020		LAV I		71.892	26.184	29.555	1.00 67.54	6
. •	MOTA	8021		VAL E		71.534	23.922	30.470	1.00 69.87	6
	MOTA	8022	С	VAL E		72.366	23.391	27.986	1.00 71.36	6
	ATOM	8023	0	VAL I		71.508	23.867	27,234	1.00 71.74	8 7
	MOTA	8024	N	THR I	E 184	72.490	22.087	28.202		-
45	ATOM	8025	CA	THR I		71.586	21.134	27.551	1.00 73.71 1.00 72.73	6 6
	ATOM	8026	CB	THR I		72.339	19.902	26.988 25.957	1.00 72.73	8
	MOTA	8027		L THR		73.243	20.327	26.392	1.00 72.00	6
	MOTA	8028		2 THR		71.353	18.897 20.656	28.565	1.00 75.19	6
	MOTA	8029	C		E 184	70.547 70.862	20.050	29.740	1.00 75.50	8
50	MOTA	8030			E 184 E 185	69.307		28.110		7
	MOTA	8031			E 185	68.234		28.992		6
	MOTA	8032			E 185	67.084		29.004	_	6
	MOTA	8033			E 185	67.547		29.285		6
55	ATOM	8034 8035		1 TYR		68.203		28.304		6
J	MOTA MOTA	8036		1 TYR		68.666		28.559	1.00 79.16	6
	MOTA	8037			E 185	67.361		30.544		6
	MOTA	8038			E 185	67.822				6
	MOTA	8039			E 185	68.472				6
60	MOTA	8040		TYR	E 185	68.919				8
	MOTA	8041	. С	TYR	E 185	67.725	18.723	28.516	1.00 77.68	б

	WO 01/58	3951							PCT/EP01/01	457
						-204				•
	MOTA	8042		TYR E 185		67.578	18.509	27.314	1.00 76.95	8 7
	MOTA	8043		SER E 180		67.460	17.831	29.463	1.00 79.15 1.00 80.95	6
	MOTA	8044		SER E 18		66.968	16.497	29.134 30.423	1.00 80.33	6
_	MOTA	8045		SER E 18		66.593	15.755 16.580	31.254	1.00 83.29	8
5	MOTA	8046		SER E 18		65.784 65.770	16.594	28.192	1.00 81.27	. 6
	MOTA	8047		SER E 18		65.612	15.764	27.291	1.00 81.31	8
	MOTA	8048		SER E 18 CYS E 18		64.948	17.624	28.402	1.00 82.15	7
	MOTA	8049		CYS E 18		63.753	17.876	27.583	1.00 83.38	6
10	ATOM ATOM	8050 8051		CYS E 18		64.119	18.104	26.143	1.00 83.62	6
10	MOTA	8052		CYS E 18		63.463	17.631	25.206	1.00 82.88	8
	ATOM	8053		CYS E 18		63.043	19.179	27.993	1.00 83.49	6
	MOTA	8054		CYS E 18		63.980	20.757	27.703	1.00 86.50	16
	ATOM	8055	N	CYS E 18		65.204	18.841	25.993	1.00 84.35	7 6
15	ATOM	8056	CA	CYS E 18		65.589	19.318	24.701	1.00 84.60 1.00 84.20	6
	MOTA	8057	С	CYS E 18		67.013	18.991	24.213	1.00 84.20	8
	MOTA	8058	0	CYS E 18		68.012	19.334 20.833	24.874 24.759	1.00 85.11	6
	MOTA	8059	CB	CYS E 18		65.319 63.808		25.731	1.00 88.15	16
	MOTA	8060	SG	CYS E 18		67.108	18.340	23.732	1.00 83.48	7
20	MOTA	8061	N	PRO E 18		65.864	18.064	22.267	1.00 82.84	6
	MOTA	8062	CD CA	PRO E 18		68.292	17.878	22.267	1.00 81.51	6
	MOTA	8063 8064	CB	PRO E 18		67.738	17.666	20.853	1.00 82.30	6
	MOTA MOTA	8065	CG	PRO E 18		66.345	17.173	21.119	1.00 82.79	6
25	ATOM	8066	C	PRO E 1		69.547	18.782	22.249	1.00 79.46	6
20	ATOM	8067	ō	PRO E 1		70.592	18.398	22.785	1.00 79.36	8
	MOTA	8068	N	GLU E 1		69.450	19.961	21.629	1.00 76.55 1.00 74.34	7 6
	MOTA	8069	CA	GLU E 1		70.592	20.878	21.529	1.00 74.34	6
	MOTA	8070	CB	GLU E 1		70.358	21.881	20.401 19.239	1.00 70.82	6
30	MOTA	8071	CG	GLU E 1		69.520	21.352 20.533	18.231	1.00 81.75	6
	MOTA	8072	CD	GLU E 1		70.336	20.965	17.884	1.00 81.85	8
	MOTA	8073		GLU E 1	90	71.471 69.836	19.472	17.775	1.00 80.52	8
	MOTA	8074		GLU E 1		70.822	21.663	22.815	1.00 71.33	6
0.5	MOTA	8075	C	GLU E 1		70.095	21.489	23.791	1.00 71.05	8
35	MOTA	8076 8077		ALA E 1		71.826	22.543	22.798	1.00 68.78	7
	MOTA	8077			91	72.142	23.390	23.957	1.00 67.15	6
	MOTA MOTA	8079		ALA E 1		73.651	23.536	24.108	1.00 65.15	6
	MOTA	8080		ALA E 1		71.502	24.787	23.836	1.00 65.83	6 8
40	MOTA	8081		ALA E 1		71.379	25.340	22.730	1.00 64.00 1.00 64.83	7
	MOTA	8082		TYR E 1	192	71.097	25.355	24.971	10	
	MOTA	8083	CA	TYR E 1	L92	70.487	26.678	24.964 25.450	1.00 63.81	
	MOTA	8084	L CB	TYR E	192	69.025		24.462		
	MOTA	8085	5 CG	TYR E	192	68.096 67.939				6
45	MOTA	808		1 TYR E	192	67.146				6
	MOTA	808		1 TYR E : 2 TYR E :		67.435		_	1.00 62.60	6
	MOTA	8088				66.642			1.00 64.04	
	MOTA	808		TYR E		66.505			1.00 64.71	. 6
50	MOTA	809 809				65.744		21.538	1.00 66.46	8
50	MOTA MOTA			TYR E		71.262				6
	ATOM			TYR E	192	71.183				
	ATOM			GLU E	193	72.010				L 7
	ATOM			GLU E	193	72.792) 6 9 6
55				GLU E		73.643	30.372			
-	ATOM			GLU E	193	74.72				9 6
	MOTA		8 CI	GLU E	193	75.62		_		
	ATOM		9 OE	1 GLU E	193	76.08				8 8
_	ATOM			2 GLU E		75.88 71.89				8 6
60				GLU E		71.89 70.74		_		
	MOTA	1 810	2 0	GUU E	173	, 0 . , 4				

,	WO 01/589	951						PCT/EP01/01457			
						-205				-	
	ATOM	8103	N	ASP E		72.418	31.187		1.00 62.00	7 6	
	MOTA	8104	CA	ASP E		71.683	32.168		1.00 60.31	6	
	MOTA	8105	CB	ASP E		70.644	31.480	29.235	1.00 62.01	6	
	MOTA	8106	CG	ASP E		71.268	30.749	30.413	1.00 64.58	8	
5	MOTA	8107		ASP E		71.200	29.504	30.448	1.00 66.44 1.00 64.95	8	
	MOTA	8108	OD2	ASP E	194	71.824	31.415	31.314	1.00 64.95	6	
	MOTA	8109	С	ASP E		72.637	32.989	29.193	1.00 59.24	8	
	MOTA	8110	0	ASP E		73.715	32.515	29.570	1.00 55.24	7	
-	MOTA	8111	N	VAL E		72.238	34.223	29.484	1.00 55.51	6	
10	MOTA	8112	CA	VAL E		73.029	35.121	30.311 29.763	1.00 53.92	6	
	MOTA	8113	CB	VAL E		73.019	36.555	30.752	1.00 53.32	6	
	MOTA	8114		VAL E		73.686	37.498	28.431	1.00 55.34	6	
	MOTA	8115		VAL E		73.738	36.595	31.715	1.00 56.03	6	
	MOTA	8116	С	VAL E		72.453	35.145 35.400	31.713	1.00 56.70	8	
15	MOTA	8117	0	VAL E		71.270	34.868	32.702	1.00 57.06	7	
	MOTA	8118	N	GLU E		73.292	34.870	34.077	1.00 57.01	6	
	MOTA	8119	CA	GLU E		72.834	33.673	34.821	1.00 57.41	6	
	MOTA	8120	CB	GLU E		73.402 72.908	33.555	36.238	1.00 61.42	6	
	MOTA	8121	CG	GLU E		73.533	32.383	36.968	1.00 62.69	6	
20	MOTA	8122	CD	GLU E		73.333	31.235	36.493	1.00 64.88	8	
	MOTA	8123	OE1			74.184	32.604	38.013	1.00 64.76	8	
	MOTA	8124	OE2			73.315	36.160	34.715	1.00 57.51	6	
	MOTA	8125	С	GLU E		74.518	36.427	34.755	1.00 60.16	8	
0.5	MOTA	8126	0	GLU F		72.375	36.969	35.192	1.00 55.54	7	
25	MOTA	8127	N	VAL I		72.712	38.226	35.829	1.00 54.09	6	
	MOTA .	8128	CA		± 197 ± 197	71.853	39.380	35.278	1.00 50.90	6	
	MOTA	8129	CB	LAAV .		72.241	40.685	35.932	1.00 47.64	6	
	MOTA	8130				72.030	39.471	33.782	1.00 49.59	6	
00	MOTA	8131	CG2		E 197	72.473	38.067	37.325	1.00 56.97	6	
30	MOTA	8132	C O		E 197	71.414	37.614	37.748	1.00 58.03	8	
	MOTA	8133	N	CED .	E 198	73.476	38.409	38.125	1.00 58.05	7	
	MOTA	8134 8135	CA		E 198	73.338	38.300	39.562	1.00 58.55	6	
	MOTA	8136	CB		E 198	74.550	37.584	40.174	1.00 58.65	6	
35	MOTA	8137	OG		E 198	74.556	36.209	39.811	1.00 60.87	8	
33	MOTA	8138	C		E 198	73.182	39.685	40.155	1.00 58.53	6	
	MOTA	8139	Ö	SER	E 198	74.049	40.549	40.004	1.00 59.57	8	
	MOTA MOTA	8140	N		E 199	72.060	39.895	40.823	1.00 58.51	7	
	ATOM	8141	CA	LEU	E 199	71.803	41.176	41.434	1.00 59.74	6	
40	ATOM	8142	CB	LEU	E 199	70.361	41.612	41.186	1.00 59.28	6	
40	ATOM	8143	CG		E 199	69.921	42.861		1.00 58.45	6	
	MOTA	8144		1 LEU		70.758			1.00 57.64	6	
	MOTA	8145		2 LEU	E 199	68.466			1.00 57.53	6 6	
	MOTA	8146	_	LEU	E 199	72.039			1.00 61.63 1.00 64.16	8	
45	ATOM	8147		LEU	E 199	71.226				7	
• -	MOTA	8148	N	ASN	E 200	73.163				6	
	ATOM	8149		ASN	E 200	73.486	_			6	
	MOTA	8150) CE	3 ASN	E 200	74.981				6	
	ATOM	8151	. CG	: ASN	E 200	75.355				8	
50	MOTA	8152	OI	1 ASN	E 200	74.686				7	
	MOTA	8153		2 ASN	E 200	76.42				6	
	ATOM	8154	1 C	ASN	E 200	73.048	_			8	
	MOTA	8155	5 0	ASN	E 200	73.61				7	
	MOTA	8156	5 N		E 201	72.01				6	
55			7 C		E 201	71.47	4 44.26			6	
	MOTA				E 201	70.25				6	
	MOTA				E 201	69.06				_	
	MOTA	816	0 C	D1 PHE	E 201	67.92	_				
	MOTA			D2 PHE	E 201	69.10					
60				El PHE	E 201	66.84				6	
	MOTA	816	3 C	EZ PHE	E 201	68.04	⊃ 4T.00	5 45.02.			

	WO 01/589	951								PCT/EP01/014	57
							-206				
	MOTA	8164	CZ	PHE E	201		66.905	42.072	46.488	1.00 43.86	6
	MOTA	8165	С	PHE E			71.029	43.977	48.066	1.00 53.50 1.00 53.30	6 8
	MOTA	8166	0	PHE E			71.001 70.650	42.823 45.032	48.504 48.770	1.00 55.04	7
5	MOTA	8167	N	ARG E			70.830	44.915	50.146	1.00 57.24	6
5	MOTA MOTA	8168 8169	CB	ARG E			71.399	44.898	51.084	1.00 59.58	6
	ATOM	8170	CG	ARG E			72.078	46.254	51.130	1.00 64.26	6
	ATOM	8171	CD	ARG E			73.337	46.278	51.951	1.00 65.59	6
	MOTA	8172	NE	ARG E			73.935	47.606	51.908	1.00 67.13	7 6
10	MOTA	8173	CZ	ARG E			75.140	47.891	52.386 52.942	1.00 68.53 1.00 69.03	7
	MOTA	8174		ARG E			75.870 75.612	46.930 49.129	52.303	1.00 68.11	7
	MOTA	8175	NH2	ARG E			69.321	46.121	50.499	1.00 57.27	6
	MOTA MOTA	8176 8177	0	ARG I			69.370	47.167	49.839	1.00 56.88	8
15	ATOM	8178	N	LYS I			68.528	45.974	51.551	1.00 56.76	7
	ATOM	8179	CA	LYS I	203		67.689	47.063	52.011	1.00 57.10	6
	MOTA	8180	CB	LYS I			66.755	46.583	53.109	1.00 58.42 1.00 60.29	6 6
	MOTA	8181	CG	LYS 1			65.904	47.682 47.157	53.702 54.883	1.00 64.62	6
-00	MOTA	8182	CD	LYS I	203		65.112 64.222	47.157	55.471	1.00 67.46	6
20	MOTA	8183	CE NZ	LYS :			63.171	48.696	54.504	1.00 70.79	7
	ATOM ATOM	8184 8185	C	LYS			68.623	48.101	52.603	1.00 56.53	6
	ATOM	8186	Ö	LYS			69.715	47.769	53.060	1.00 58.18	8
	ATOM	8187	N	LYS	E 204	ļ.	68.190	49.352	52.629	1.00 53.82	7 6
25	MOTA	8188	CA	LYS			69.021	50.392	53.207	1.00 52.45 1.00 50.86	6
	MOTA	8189	CB		E 204		68.545	51.766 52.110	52.731 51.279	1.00 44.94	6
	MOTA	8190	CG	LYS	E 204 E 204		68.852 68.253	53.462	50.970	1.00 45.54	6
	ATOM	8191	CD CE		E 204		68.744	54.050	49.669	1.00 46.91	б
30	ATOM ATOM	8192 8193	NZ	LYS			68.388	53.268	48.463	1.00 48.94	7
50	MOTA	8194	C	LYS			68.991	50.317	54.747	1.00 54.01	6
	ATOM	8195	0	LYS		4	68.119	49.668	55.329	1.00 54.82 1.00 53.51	8 7
	MOTA	8196	N		E 20		69.958	50.969	55.394 56.848	1.00 52.96	6
	MOTA	8197	CA		E 20		70.025 69.747	50.987 52.400	57.344	1.00 54.24	6
35	ATOM	8198	C	GLY GLY	E 20		69.326	53.224	56.507	1.00 53.02	8
	MOTA	8199 8200		2 GLY			69.937	52.697	58.551	1.00 54.73	8
	MOTA MOTA	8201				1	42.707	26.844	16.535	1.00 50.04	8
	ATOM	8202		2 WAT		2	46.115	22.922	8.819	1.00 33.72	8 8
40	MOTA	8203	ОН	2 WAT		3	49.921	22.962	13.240	1.00 27.71 1.00 48.75	8
	MOTA	8204		2 WAT		4	48.219	24.526 41.690	9.434 17.095	1.00 41.54	8
	MOTA	8205				5	27.826 24.872	36.589	8.613	1.00 51.20	8
	ATOM	8206		2 WAT		6 7	36.046			1.00 33.21	8
45	MOTA MOTA	8207 8208	OH	2 WAT 2 WAT		8	35.043	57.811	16.418	1.00 28.29	8
70	MOTA	8209		2 WAT		9	55.882		16.997		8
	MOTA	8210		2 WAT		.0	55.717				8 8
	MOTA	8211		2 WAT		.1	54.077		_		8
	MOTA	8212		2 WAT		.2	60.807				8
50		8213		2 WAT		L3 L4	66.541 64.752				8
	MOTA	8214		2 WAT 2 CA2		1	56.450			1.00 76.79	20
	MOTA MOTA	821	6 CT	1 CL1	I	2	37.092			1.00 43.91	17
	ATOM	821	7 CA-	-2 CA2	I	3	17.667				20
55		821	8 CL-	-1 CL1	I	4	20.502				17
-	MOTA	821	9 CA-	-2 CA2	I	5	16.762				20 17
	MOTA	822	0 CT-	-1 CL1	I	6	37.412				20
	MOTA	822	1 CA	2 CA2	I	7	55.038 64.026				17
60	MOTA	822	2 CL	-1 CL1 +2 CA2	. <u>1</u>	8 9	79.499			5 1.00 85.28	20
60	MOTA (MOTA	822	CA و	-1 CLI	Ī	10	64.28				17
	ATOM	022	- 02								

	WO 01/58	951				-207			PCT/EP01/0145	37
						-207 31.694	22.169	23.679	1.00109.78	6
				HEP L HEP L	1 1	32.042	22.822	25.000	1.00106.01	6
	MOTA			HEP L	1	33.258	20.667		1,00 50	6
	MOTA MOTA	-		HEP L	1	34.107	19.901	26.462		6
5	MOTA			HEP L	1	33.049	21.220	28.203	2100 3011	6 6
0	ATOM	8230	C6	HEP L	1	32.154	21.953	27.266	X	6
	ATOM	8231	C7	HEP L	1	34.051	19.067		T.00 J	6
	MOTA	8232	C8	HEP L	1	35.030	19.802			8
	MOTA	8233	04	HEP L	1	34.441	19.860			7
10	MOTA	8234	N1	HEP L	1	32.880	22.043 23.336		T.00-0	.6
	MOTA	8235	S1	HEP L	1	31.207 31.826	22.878	21.182	1.00113.59	8
	MOTA	8236	01	HEP L	1 1	31.477	24.685		1.00111.64	8
	MOTA	8237	02	HEP L	1	29.701	23.322	22.307	1.00111.51	8
4	ATOM	8238	03 N2	HEP L	1	33.333	19.839	27.737	1.00 98.16	7
15	ATOM	8239 8240	C1	HEP L	2	19.833	49.708	24.248	1.00108.88	6
	MOTA	8241	C2	HEP L	2	20.653	49.684	25.518	1.00104.63	6
	ATOM ATOM	8242	C3	HEP L	2	19.090	47.814	26.172	1.00100.27	6 6
	MOTA	8243	C4	HEP L	2	18.728	46.788	27.241	1.00 98.30 1.00100.12	6
20	ATOM	8244	C5	HEP L	2	19.702	48.326	28.859	1.00100.12	6
	MOTA	8245	C6	HEP L	2	20.022	49.380	27.845 29.663	1.00 97.02	6
	MOTA	8246	C7	HEP L	2	18.080	46.646 46.065	30.550	1.00 96.36	6
	MOTA	8247	C8	HEP L	2	19.186	46.714	31.805	1.00 95.77	8
	MOTA	8248	04	HEP L	2	19.161 20.281	48.676	26.560	1.00102.78	7
25	MOTA	8249	N1	HEP L	2	20.281	50.530	22.892	1.00112.59	16
	MOTA	8250	S1	HEP L	2 2	20.348	49.765	21.697	1.00113.24	8
	MOTA	8251	01	HED L	2	22.024	50.791	23.309	1.00111.25	8
	MOTA	8252	02	HEP L	2	20.059	51.924	22.770	1.00111.32	8
00	MOTA	8253	03 N2	HEP L	2	18.478	47.544	28.507	1.00 98.39	7
30	MOTA	8254 8255	C1	HEP L	3	42.028	70.369	23.900	1.00109.55	6
	MOTA MOTA	8256	C2	HEP L	3	42.091		25.003	1.00104.54 1.00 97.17	6 6
	MOTA	8257	C3	HEP L	3	40.178		25.988	1.00 97.17	6
	ATOM	8258	C4	HEP L	3	39.192		27.124	1.00 98.62	6
35	MOTA	8259	C5	HEP L	3	40.844	4		1.00100.28	6
-	MOTA	8260	C6	HEP L	3	41.854			1.00 97.37	6
	MOTA	8261	C7	HEP L	3	39.103			1.00 97.34	6
	MOTA	8262			3	38.600 39.310			1.00 95.42	8
	MOTA	8263			3 3	41.104			1.00100.25	7
40	MOTA	8264		_	3	42.85			1.00113.40	16
	MOTA	8265			3	41.999		21.301	1.00112.83	8
	MOTA	8266		_		43.21		22.535	1.00111.97	8
	MOTA	8267 8268				44.20	8 70 <i>.</i> 580	22.342	1.00111.22	8
45	MOTA MOTA					39.98	2 70.75	28.394	1.00 97.91	7 6
45	ATOM					67.84				6
	MOTA					67.69				6
	MOTA				, 4	67.44		8 25.071 6 26.150		6
	MOTA			4 HEP I		67.19	_			6
50						68.22				6
	ATOM		5 C.			68.52		_		6
	MOTA	827				68.12				6
	ATOM					67.28 68.17			1.00100.41	8
	MOTA	_				67.47			1.00103.08	7
55		827				67.55			1.00112.53	16
	MOTA			1 HEP	-	66.82		0 20.813	3 1.00112.71	8
	MOTA			1 HEP :		67.03		30 22.59		8
	OTA			3 HEP		68.9	o8 52.7€	55 21.42		8
6	IOTA IOTA (12 HEP		68.2	58 57.35			7 6
O'	OTA U			1 HEP		62.83	36 24.32	27 23.51	1 1.00108.64	
	ALU	0_0								

	WO 01/5	8951						PCT/EP01/01457				
							-208					
	MOTA MOTA MOTA	8286 8287 8288	C2 C3 C4	HEP HEP HEP HEP	L L	5 5 5 5	62.164 64.426 65.270 63.215	25.268 25.352 25.934 26.126	24.495 25.555 26.676 27.960		-	6 6 6
5	ATOM ATOM ATOM ATOM	8289 8290 8291 8292	C5 C6 . C7 C8	HEP HEP HEP	L L	5 5 5	62.366 65.381 65.085	25.505 26.089 27.500	26.903 29.165 29.708	1.00	00.20 98.56 98.97 98.36	6 6 6 8
10	MOTA MOTA MOTA MOTA MOTA MOTA	8293 8294 8295 8296 8297 8298	04 N1 S1 01 02 03	HEP HEP HEP HEP HEP	L L L	5 5 5 5 5 5 5	64.379 63.001 61.935 62.912 60.852 61.166	27.406 25.830 24.146 24.120 25.151 22.846	30.942 25.594 21.985 20.912 22.006 22.024	1.001 1.001 1.001 1.001	.01.58 .12.71 .12.36 .11.63	7 16 8 8 8
15	ATOM END	8299	N2	HEP	L	5	64.610	25.582	27.957	1.00	98.40	7
			Ator Type	-	idue	<u>#</u>	$\bar{\mathbf{x}}$	¥	<u>z</u>	<u>occ</u>	<u>B</u>	

25

Table 1: Structural coordinates of AChBP

"Atom type" refers to the element whoose coordinate are measured. The first letter in the column defines the element.

"Residue" refers to the amino acid in the AChBP protein sequence, using the standard three letter abbreviations known in the art.

"#" refers to the residue number.

"X, Y, Z" crystallographically define the atomic position, in three-dimensional space, of the element measured.

"OCC" is the occupancy volume.

30 "B" is a thermal factor that measures movement of the atom around its atomic center.

-209 Claims

 A water-soluble protein derived from a mollusc being capable of binding a ligand of a ligand-gated receptor.

5

20

- 2. The protein of claim 1, wherein the ligand is acetylcholine, gamma-amino-butyric acid (GABA), glycine or serotonin.
- The protein of claim 2, wherein said protein is a acetylcholine-binding protein(AChBP).
 - 4. The protein of any one of claim 1 to 3 which is capable of forming multimers.
- The protein of any one of claims 1 to 4 which is derived form a Pulmonata
 species, preferably from a Basommatophora species.
 - 6. The protein of any one of claims 1 to 5 comprising an amino acid sequence selected from the group consisting of:
 - (a) an amino acid sequence as depicted in any one of SEQ ID Nos. 2, 4,
 6 or 8 or a functional equivalent thereof, or a fragment of at least 5
 continuous amino acids thereof;
 - (b) an amino acid sequence having at least 30% amino acid identity to the amino acid sequence of any one of SEQ ID Nos. 2, 4, 6 or 8.
- 25 7. A water-soluble ligand binding protein capable of binding a ligand of a ligand-gated receptor and comprising at least 5 continuous amino acids of the aminoacid sequence depicted in any one of SEQ ID Nos. 2, 4, 6 or 8 and/or said protein is detectable by a monoclonal or polyclonal antibody which recognises, preferably with a binding affinity of at least 10⁻⁷M, a protein of any one of claims 1 to 6.
 - 8. A water-soluble protein being capable of binding a ligand of a ligand-gated receptor comprising
- (a) at least the amino acids of the water-soluble protein of any one of
 35 claims 1 to 6 determining solubility of said protein, in the same or
 corresponding positions as in said protein; and
 - (b) at least 4 amino acids determining binding to said ligand.

-210

- 9. The protein of claim 7 or 8 which is capable of forming multimers.
- 10. The protein of any one of claims 7 to 9 comprising 200-240 amino acids.

5

- 11. The protein of any one of claims 7 to 10, wherein the ligand is acetylcholine, nicotine, lophotoxin, d-tubocurarine, carbamylcholine, galanthamine or epibatidine.
- 10 12. The protein of any one of claims 1 to 11, wherein said ligand-gated receptor is derived from an arthropod (preferably insect), a plant (preferably a higher plant, most preferably a seed plant) or a chordate (preferably a mammalian, most preferably human).
- 15 13. The protein of any one of claims 7 to 12, wherein said ligand-gated receptor is a nicotinic acetylcholine receptor.
- 14. The protein of any one of claims 7 to 13, wherein said amino acids determining solubility are in the same positions as in the AChBP having the amino acid sequence as depicted in any one of SEQ ID Nos. 2, 4, 6 or 8; preferably in which said solubility-determining amino acids comprise solvent accessible regions in the crystal structure according to Figure 10.
- The protein of any one of claims 7 to 14 comprising an amino acid sequence having at least 40% amino acid identity to the amino acid sequence 20-223 of any one of SEQ ID Nos. 2, 4, 6 or 8, in which the ligand binding amino acids have been replaced with the corresponding amino acids of a ligand-gated receptor.
- The protein of any one of claims 7 to 15, in which said solubility-determining amino acids (a) comprise hydrophilic amino acids (Asp, Glu, Arg, Lys) from the sequences 20-44, 73-81, 86-92, 112-120, 135-152, 166-189, 196-20, 209-213, and/or 219-227 of SEQ ID No. 2.
- 35 17. The protein of claim 16, in which said solubility determining amino acids (a) comprise amino acids Asp(36), Asp(68), Glu(115), Arg(137), Asp(143), Asp(148), Glu(150), Arg(167), Arg(189), Glu(215) of SEQ ID No.2, wherein

-211

Asp may be exchanged for Glu and vice versa and Lys may be exchanged for Arg and vice versa.

- 18. The protein of any one of claims 7 to 17 which further comprises the amino acids Cys(142), Thr(149), Ala(153), Thr(154), Cys(155), Arg(156), Ile(157) and/or Lys(158) of SEQ ID No. 2.
- 19. The protein of any one of claims 7 to 17 which comprises the amino acids (b) Pro(39), Trp(77), Trp(101), Pro(103), Asp(194), and/or Ser(161) of SEQ ID
 10 No. 2.
 - 20. The protein of any one of claims 7 to 19 in which the amino acid sequences 165-169 and/or 200-203 of SEQ ID No. 2 have been exchanged with the corresponding sequence of the ligand-gated receptor.
- The protein of any one of claims 7 to 20 which is capable of binding a ligand of an acetylcholine receptor, in which at least one of the amino acid sequences Trp(101) Tyr(T08), Trp(162) His(164) and Tyr(204) Tyr(211) of SEQ ID No. 2 have been exchanged with the corresponding sequence of the acetylcholine receptor.
- 22. A method for the production of a water-soluble ligand-gated receptor or a corresponding ligand-binding domain or for improving the water solubility and accessibility to crystallization of such a receptor or domain, said method comprising altering the amino acid sequence of the extracellular domain of a ligand-gated receptor by way of substituting, adding, deleting or modifying at least one amino acid at a position corresponding to an amino acid determining or contributing to the water-solubility of the protein of any one of claims 1 to 21.
- The method of claim 22, wherein the ligand-gated receptor is defined as in any one of claims 1 to 21.
- The method of claim 22 or 23, wherein at least one amino acid is altered to the corresponding amino acid of the amino acid sequence depicted in any one of SEQ ID Nos. 2, 4, 6 or 8, or to a an equivalent amino acid, preferably

30

WO 01/58951 PCT/EP01/01457

-212

in which said solubility-determining amino acids comprise solvent accessible regions in the crystal structure according to Figure 10.

- The method of any one of claims 22 to 24, wherein loop Cys123-Cys136 of
 SEQ ID No. 2 is inserted into the corresponding region of the ligand binding domain of the ligand-gated receptor.
 - 26. The method of any one of claims 22 to 25 further comprising
- (a) culturing a host cell transfected with and capable of expressing a
 polynucleotide comprising a nucleotide sequence encoding the altered amino acid sequence; and optionally
 - (b) recovering said water-soluble ligand-gated receptor or corresponding ligand-binding domain from the culture.
- 15 27. A water-soluble ligand-gated receptor or ligand-binding domain obtainable by the method of any one of claims 22 to 26.
 - 28. The protein of any one of claims 1 to 21 or 27 further comprising a spacer sequence allowing coupling with a carrier body.
 - 29. A fusion protein comprising the water-soluble ligand-binding protein of any one of claims 1 to 21, 27 or 28, or a binding fragment thereof and a fragment of a ligand-gated receptor
- 25 30. A dimer or pentamer consisting of at least one monomer comprising a protein of any one of claims 1 to 21 or 27 to 29.
 - 31. A ligand-gated ion channel comprising a protein of any one of claims 1 to 21 or 27 to 29 or the dimer or pentamer of claim 30.
 - 32. One or more polynucleotides encoding the protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31.
- 35 33. The polynucleotide(s) of claim 32 which comprise(s)

20

30

35

WO 01/58951 PCT/EP01/01457

-213

- (a) a nucleotide sequence having at least 15 continuous nucleotides of the nucleotide sequence depicted in any one of SEQ ID Nos. 1, 3, 5 or 7 or a degenerated sequence thereof; or
- (b) a nucleotide sequence capable of hybridizing to a nucleotide sequence of (a) under stringent hybridisation conditions.
- 34. The polynucleotide(s) of claim 32 or 33 which is(are) operatively linked to heterologous expression control sequences allowing expression inprokaryotic or eukaryotic cells.
- 35. One or more vector(s) containing the polynucleotide(s) of any one of claims32 to 34.
- 36. A host cell genetically engineered with the polynucleotide(s) of any one claims
 32 to 34 or with the vector(s) of claim 35.
 - 37. An antigen comprising an epitope of at least 5 continuous amino acids of the amino acid sequence depicted in any one of SEQ ID Nos. 2, 4, 6 or 8 and/or said epitope is detectable by a monoclonal or polyclonal antibody which recognises, preferably with a binding affinity of at least 10⁻⁷M, a protein of any one of claims 1 to 6.
- An antibody specifically recognizing the protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30, the ligand-gated ion channel of claim 31 or the antigen of claim 37.
 - 39. An oligonucleotide probe comprising a nucleotide sequence having at least 15 continuous nucleotides of a polynucleotide of any one claims 32 to 34 or encoding the antigen of claim 37.
 - 40. A composition comprising the protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30, the ligand-gated ion channel of claim 31, the polynucleotide(s) of any one claims 32 to 34, the vector(s) of claim 35, the host cell of claim 36, the antigen of claim 37, the antibody of claim 38, or an oligonucleotide probe of claim 39; and optionally suitable means for detection or performing a ligand-receptor binding assay.

15

30

35

WO 01/58951 PCT/EP01/01457

41. A method for identifying an agonist/activator or antagonist/inhibitor of a ligand-gated receptor comprising the steps of:

-214

- (a) contacting the water-soluble ligand-binding protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30, the ligand-gated ion channel of claim 31 or a cell expressing said protein in the presence of components capable of providing a detectable signal in response to ligand binding with a compound to be screened under conditions that permit binding of said compound to the ligand-binding protein; and
- 10 (b) detecting the presence or absence of a signal generated from the binding activity of the ligand-binding protein, wherein the presence/increase and absence/decrease of the signal is indicative for an agonist/activator and antagonist/inhibitor, respectively, of a ligand-gated receptor.
 - 42. A crystal of a protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31.
- 43. A crystal of a protein-ligand complex comprising a protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31; and a ligand.
 - 44. The crystal of claim 43, wherein the ligand comprises an N-alkylated hydroxyalkyl and/or a quaternary ammonium ion.
- 45. The crystal of claim 43, wherein the ligand comprises 4-(2-Hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES), B-bippinatin, lophotoxin, d-tubocurarine, carbamylcholine, galanthamine, epibatidine or alphabungarotoxin.
 - 46. The crystal of any one of claims 42 to 45, wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein or protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms.
 - 47. The crystal of any one claims 42 to 46, wherein the protein has an amino acid sequence of amino acids 20 to 223 of SEQ ID No. 2, or an amino acid

35

WO 01/58951 PCT/EP01/01457

-215

sequence that differs from amino acid 20 to 223 of SEQ ID No. 2 by only having conservative substitutions.

48. The crystal of claim 47, wherein the ligand is HEPES.

49. The crystal of claim 46 having (1) a space group of P2₁2₁2₁ and a unit cell of dimensions of a=120.6Å, b=137.0Å and c=161.5Å; (2) a space group of P4₂2₁2 and a unit cell of dimensions of a=b=141.6Å and c=120.8Å or (3) a space group of P2₁ and a unit cell of dimensions of a=121.1Å, b=162.1Å, c=139.4Å, β=90.1°.

- 50. The crystal of any one of claims 42 to 49, wherein the protein has secondary structural elements that include .alpha.-helix and antiparallel .beta.-sheets as shown in Figure 7, 10, 11 and/or 12.
- The crystal of any one claims 42 to 50 having a three-dimensional structure as defined by atomic coordinates shown in Table 1.
- 52. The crystal of any one of claims 42 to 51 having a binding cavity as shown in Figure 6, 8, 9 and/or 13.
 - 53. A method of using the crystal of any one of claims 42 to 52 in a drug screening assay comprising:
- (a) selecting a potential ligand by performing structure assisted drug

 design with the three-dimensional structure determined for the crystal, wherein said selecting is performed in conjunction with computer modeling; optionally
 - (b) contacting the potential ligand with the ligand binding domain of the ligand-gated receptor in an in vitro or in vivo assay; and
- 30 (c) detecting the binding of the potential ligand for the ligand binding domain.
 - 54. The method of claim 53, wherein the ligand-gated receptor is a nicotinic acetylcholine receptor.
 - 55. The method of claim 53 or 54 further comprising:

35

PCT/EP01/01457 WO 01/58951 -216 forming a supplemental crystal of a protein-ligand complex by co-(d) crystallization or soaking the crystal of the water-soluble ligand-binding protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31, with a potential drug, wherein the crystal effectively diffracts X-rays for the 5 determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms, more preferably greater than 3; determining the three-dimensional structure of the supplemental (e) 10 crystal; selecting a candidate drug by performing a structure assisted drug (f) design with the three-dimensional structure determined for the supplemental crystal, wherein said selecting is performed in conjunction with computer modeling; optionally contacting the candidate drug with a cell that expresses the ligand-15 (g) gated receptor; and detecting a cell response; wherein a candidate drug is identified as (h) a drug when the cell response is altered compared to a cell that has not been contacted with the candidate compound. 20 The method of any one of claims 53 to 55 further comprising an initial step 56. that precedes step (a) wherein said initial step consists of determining the three-dimensional structure of a crystal comprising a protein-ligand complex formed between the water-soluble ligand-binding protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion 25 channel of claim 31, and the ligand of the ligand-gated receptor, wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms. 30 A method of growing a crystal of a protein-ligand complex comprising: 57. contacting the water-soluble ligand-binding protein of any one of (a) claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31 with a ligand of a ligandgated receptor, wherein the water-soluble ligand-binding protein

forms a protein-ligand complex with the ligand; and

WO 01/58951 PCT/EP01/01457

-217

(b) growing the crystal of the protein-ligand complex; wherein the crystal effectively diffracts X-rays for the determination of the atomic coordinates of the protein-ligand complex to a resolution of greater than 5.0, preferably greater than 4.0 Angstroms.

5

- 58. A drug screening assay comprising soaking the crystal of any one of claims 42 to 52 in a solution of compounds to be screened and detecting the binding of the compound to the ligand-binding protein.
- 10 59. The method of claim 57 or 58, wherein said ligand comprises an alkylated nitrogen and/or quaternary ammonium ion.
 - 60. A method of increasing or decreasing the affinity of a drug to a ligand-gated receptor, comprising

15

(a) performing structure assisted drug design with the three-dimensional structure determined for the crystal of any one of claims 42 to 52, wherein said drug design is performed in conjunction with computer modeling; and

20

- (b) modifying said drug to alter or eliminate a portion thereof suspected of interacting with a binding site of the binding cavity or with a non-specific binding site of the protein in the crystal.
- 61. The method of claim 60, wherein step (a) further comprises the steps of a method of any one of claims 53 to 59.

25

- 62. The method of claim 60 or 61, further comprising after step (b), the additional step of:
 - (c) repeating the method used to perform structure assisted drug design according to step (a) using the modified drug according to step (b).

30

35

63. A method of drug design comprising the step of using the structural coordinates of a water-soluble ligand-binding protein crystal comprising the coordinates of Table 1, to computationally evaluate a chemical entity for associating with the ligand-binding site or a non-specific binding site of a ligand-binding protein.

PCT/EP01/01457 WO 01/58951 -218

- The method of any one of claims 53 to 63, wherein the identified drug 64. prevents or promotes correct assembly of a ligand-gated ion channel.
- The method of any one of claims 53 to 63, wherein the identified drug binds to 65. a non-specific binding site of a ligand-gated ion channel. 5
 - The method of any one of claims 53 to 65 further comprising synthesizing the 66. drug in a therapeutically effective amount.
- A drug produced by the method of claim 66 or a pro-drug thereof. 10 67.
- The drug of claim 67 which interacts with a ligand-gated receptor comprising 68. a pentamer of claim 30 with monomers A to E, wherein the drug binds to one or more primary contact regions of a monomer (residues from A contacting B) defined by amino acid residues 15 to 21, 44 to 47, 85 to 87, 91 to 94, 122 to 15 124, 143 to 146, 149, 185 to 187 of the mature protein of SEQ ID No. 2 and/or to one or more of the complementary contact regions of the other monomer (from B contacting A, (identical to residues on A contacting E) defined by amino acid residues 3 to 4, 7 to 8, 11, 37 to 39, 53, 75 to 77, 96 to 104, 114 to 118 and 163-170 of the mature protein of SEQ ID No. 2; or to the contact 20 regions as identified in Figure 14; or to the corresponding contact regions of the monomers of a ligand-gated ion channel.
- The drug of claim 68, wherein the ligand-gated ion channel is the nicotinic 69. acetylcholine receptor and the order of the monomers is $\alpha\gamma\alpha\beta\delta$. 25
- A computer readable medium comprising a nucleotide sequence of the 70. polynucleotide(s) of any one of claims 32 to 34, an amino acid sequence of a protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30 or the ligand-gated ion channel of claim 31, or the structural 30 coordinates of a crystal of any one of claims 40 to 50.
 - A device comprising the computer readable medium of claim 70. 71.
- Use of the computer readable medium of claim 70 or the device of claim 71 35 72. for modeling an antagonist/inhibitor or agonist/activator of a ligand-gated receptor.

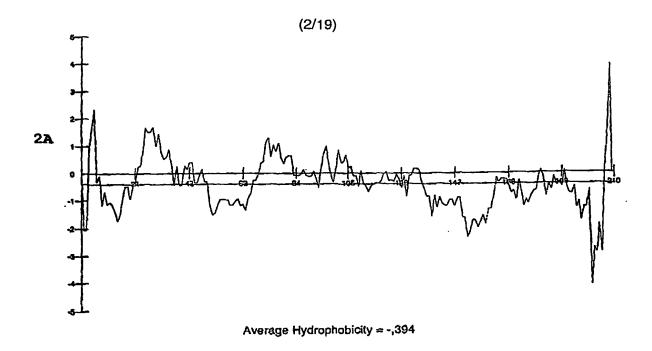
PCT/EP01/01457

- 73. Use of the crystal of any one of claims 42 to 52 or its structural coordinates as a template for modeling the 3D structure of a ligand-gated ion channel.
- 5 74. Use of the polynucleotide(s) of any one of claims 32 to 34, the protein of any one of claims 1 to 21 or 27 to 29, the dimer or pentamer of claim 30, the ligand-gated ion channel of claim 31, the vector(s) of claim 35, the host cell of claim 36, the antigen of claim 37, the antibody of claim 38, an oligonucleotide probe of claim 39, the crystal of any one of claims 42 to 52 or a method of any one of claims 53 to 66 for screening or profiling putative ligands of ligand-gated receptors.
- Use of an antagonist/inhibitor or agonist/activator identified according to a method of any one of claims 53 to 66 for the preparation of a pharmaceutical composition for the treatment of a ligand-gated ion channel mediated or related disorder.
- 76. The use of claim 75, wherein the antagonist/inhibitor is or is derived from the protein of any one of claims 1 to 21 or 27 to 29, an antigen of claim 37, an antibody of claim 38 or from a toxin of the ligand-gated ion channel.
 - 77. The use of claim 75, wherein the agonist/activator is or is derived from a the protein of any one of claims 1 to 21 or 27 to 29, an antigen of claim 37, an antibody of claim 38 or from epibatidine, acetylcholine, choline, nicotine, carbachol, serotonin or GABA.
- 78. The use of any one claims 75 to 77, wherein the ligand-gated ion channel is the nicotinic acetylcholine receptor and said mediated or related disorder is Tourette's syndrome, Alzheimer's disease, addiction to nicotine or schizophrenia.
 - 79. Use of ligand of a ligand-gated receptor for identifying and isolating a water-soluble ligand-binding protein from a mollusc.
- 35 80. The use of claim 79, wherein said ligand is α -bungarotoxin.

(1/19)

L-AChBP_T1. L-AChBP_T2. B-AChBP_T1. B-AChBP_T2.	MRRNIFCLACLWIVQACLSLDRADILYNIRQTSRPDVIPTQRDRPVAVSVSLKFINILMRRNIFCLACLWIVQGCLSLDRADILYNIRQTSRPDVIPTQRDRPVAVSVSLKFINIL MAELRRIILLLCTIAFHVSHGQIRWTLLNQITGESDVIPLSNNTPLNVSLNFKLMNIV MAELRGIILLLCTIAFHVSHGQIRWTLLNQITGESDVIPLSNNTPLNVSLNFKLMNIL * *: * * : : : : : : : : : : : : : : :
L-AChBP_T1. L-AChBP_T2. B-AChBP_T1. B-AChBP_T2.	EVNEITNEVDVVFWQQTTWSDRTLA-WNSSHSPDQVSVPISSLWVPDLAAYNAISKPEVL EVNEITNEVDVVFWQQTTWSDRTLA-WNSSHSPDQVSVPISSLWVPDLAAYNAISKPEVL EADTEKDQVEVVLWTQASWKVPYYSSLLSSSSLDQVSLPVSKMWTPDLSFYNAIAAPELL EADTEKDQVEVVLWTQASWKVPYYSSLLSSSSLDQVSLPASKMWTPDLSFYNAIAAPELL *.: .::*:**: *::*. : ** * ****: **::* **:: ***:
L-AChBP_T1. L-AChBP_T2. B-AChBP_T1. B-AChBP_T2.	TPQLARVVSDGEVLYMPSIRQRFSCDVSGVDTESGATCRIKIGSWTHHSREISVDPTTE- TPQLARVVSDGEVLYMPSIRQRFSCDVSGVDTESGATCRIKIGSWTHHSGEISVDPTTE- SADRVVVSKDGSVIYVPSQRVRFTCDLINVDTEPGATCRIKVGSWTHDNKQFALITGEEG STDRVVVSKDGSVIYVPSQRVRFTCDLINVDTEPGATCRIKVGSWTFDNKQLALITGEEG :.: . * .**.*:*: * * **:**: . **********
L-AChBP_T1. L-AChBP_T2. B-AChBP_T1. B-AChBP_T2.	NSDDSEYFSQYSRFEILDVTQKKNSVTYSCCPEAYEDVEVSLNFRKKGRSEIL NSDDSEYFSQYSRFEILDVTQKKNSVIYSCCPEAYEDVEVSLNFRKKGRSEIL VVNIAEYFDS-PKFDLLSATQSLNRKKYSCCENMYDDIEITFAFRKK VVNIAEYFDS-PKYDLLSATQSLNRKKYRCCENMYEDIEITFAFRKK : :***:::***. * * * * : *:*:::: ****

Figure 1



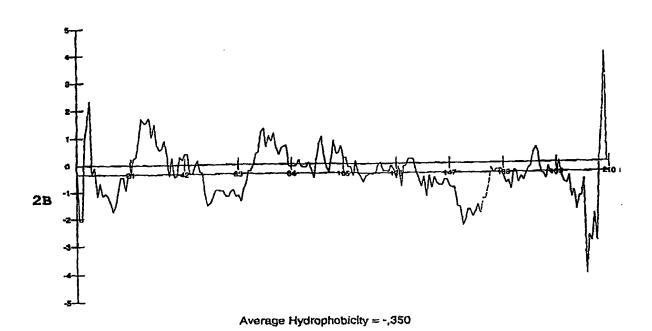
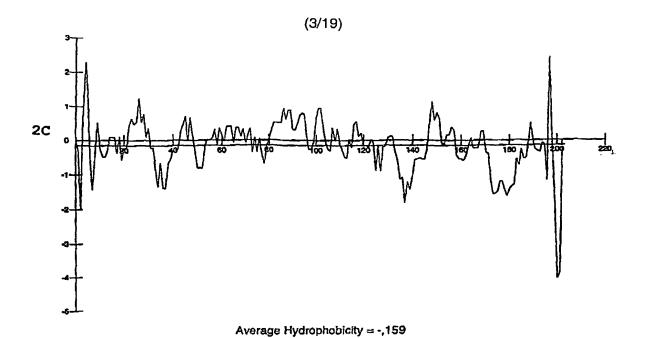


Figure 2



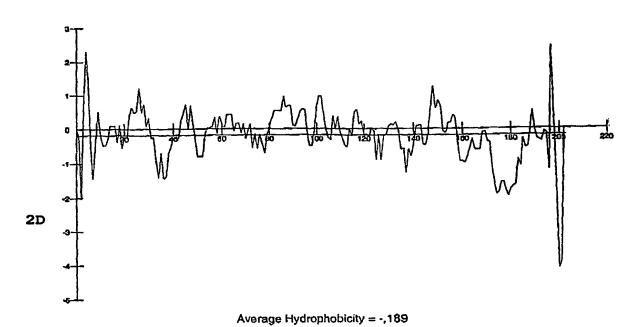


Figure 2 (continued)

(4/19)

L-AChBP_T1 L-AChBP_T2 B-AChBP_T1 B-AChBP_T2 h_nAChR_A7 h_5HT3 h_GlyR_a1 h_GABAA_b1	LDRADILYNIRQTSRPDVIPTLDRADILYNIRQTSRPDVIPTQIRWTLLNQITGESDVIPLQIRWTLLNQITGESDVIPL
L-AChBP_T1 L-AChBP_T2 B-AChBP_T1 B-AChBP_T2 h_nAChR_A7 h_5HT3 h_GlyR_a1 h_GABAA_b1	QRDR-PVAVSVSLKFINILEVNEITNEVDVVFWQQTTWSDRTLAWNSSHSPDQVSVPI QRDR-PVAVSVSLKFINILEVNEITNEVDVVFWQQTTWSDRTLAWNSSHSPDQVSVPI SNNT-PLNVSLNFKLMNIVEADTEKDQVEVVLWTQASWKVPYYSS-LLSSSSLDQVSLPV SNNT-PLNVSLNFKLMNILEADTEKDQVEVVLWTQASWKVPYYSS-LLSSSSLDQVSLPA ANDSQPLTVYFSLSLLQIMDVDEKNQVLTTNIWLQMSWTDHYLQWNVSEYPGVKTVRFPD RDWRKPTTVSIDVIVYAILNVDEKNQVLTTYIWYRQYWTDEFLQWNPEDFDNITKLSIPT FKGP-PVNVSCNIFINSFGSIAETTMDYRVNIFLRQQWNDPRLAYNEYPDDSLDLDPSML LGER-VTEVKTDIFVTSFGPVSDHDMEYTIDVFFRQSWKDERLKF-KGPMTVLRLNNLMA
L-AChBP_T1 L-AChBP_T2 B-AChBP_T1 B-AChBP_T2 h_nAChR_A7 h_5HT3 h_GlyR_a1 h_GABAA_b1	SSLWVPDLAAYNAISK-PEVLTPQLARVVSDGEVLYMPSIRQRFSCDVSG-VDTESGA SSLWVPDLAAYNAISK-PEVLTPQLARVVSDGEVLYMPSIRQRFSCDVSG-VDTESGA SKMWTPDLSFYNAIAA-PELLSADRVVVSKDGSVIYVPSQRVRFTCDLIN-VDTEPGA SKMWTPDLSFYNAIAA-PELLSTDRVVVSKDGSVIYVPSQRVRFTCDLIN-VDTEPGA GQIWKPDILLYNSADERFDATFHTNVLVNSSGHCQYLPPGIFKSSCYIDVRWFPFDVQ DSIWVPDILINEFVDV-GKSPNIPYVYIRHQGEVQNYKPLQVVTACSLDIYNFPFDVQ DSIWKPDLFFANEKGAHFHEITTDNKLLRISRNGNVLYSIRITLTLACPMDLKNFPMDVQ SKIRTPDTFFHNGKKSVAHNMTMPNKLLRITEDGTLLYTMRLTVRAECPMHLEDFPMDAH : ** :
L-AChBP_T1 L-AChBP_T2 B-AChBP_T1 B-AChBP_T2 h_nAChR_A7 h_5HT3 h_GlyR_a1 h_GABAA_b1	TCRIKIGSWTHHSREISVDPTTE-NSDDSEYFSQYSRFEILDVTQKKNSVTYSCCPE TCRIKIGSWTHHSGEISVDPTTE-NSDDSEYFSQYSRFEILDVTQKKNSVIYSCCPE TCRIKVGSWTHDNKQFALITGEEGVVNIAEYFDS-PKFDLLSATQSLNRKKYSCCEN TCRIKVGSWTFDNKQLALITGEEGVVNIAEYFDS-PKYDLLSATQSLNRKKYRCCEN HCKLKFGSWSYGGWSLDLQMQEADISGYIPN-GEWDLVGIPGKRSERFYECCKE NCSLTFTSWLHTIQDINISLWRLPEKVKSDRSVFMNQ-GEWELLGVLPYFREFSMESS-N TCIMQLESFGYTMNDLIFEWQEQGAVQVADGLTL-PQFILKEEKDLRYCTKHYNT-G ACPLKFGSYAYTRAEVVYEWTR-EPARSVVVAEDGSRLNQYDLLGQTVDSGIVQSSTG *:.*::
L-AChBP_T1 L-AChBP_T2 B-AChBP_T1 B-AChBP_T2 h_nAChR_A7 h_5HT3 h_GlyR_a1 h_GABAA_b1	AYEDVEVSLNFRKKGRSEIL AYEDVEVSLNFRKKGRSEIL MYDDIEITFAFRKK MYEDIEITFAFRKK PYPDVTFTVTMRRRTLYYGL YYAEMKFYVVIRRPLFYVV KFTCIEARFHLERQMGYYLI EYVVMTTHFHLKRKIGYFVI : : ::::

Figure 3

(5/19)

nAChR_h-A2	MGPSCPVFLSFTKLSLWWLLLTPAGGEEAKRPPPRAPGDPLSSPSPTALPQGGSHTE
nAChR_h-A4	MELGGPGAPRLLPPLLLLLGTGLLRASSHVE
nAChR_h-A5	MAARGSGPRALRLLLLVQLVAGRCGLAGAAGGAQRGLSEPS
nAChR_h-A3	LLLSLLPVARASE
nAChR_h-A6	WLCVFTPFFKGCVGCA
nAChR_h-A1	EFSLCSAGLVLGSE
nAChR_h-A7	HVSLQG-EFQR
nAChR_h-A9	AAETADG-KYAQ
B-AChBP_T1	IAFHVSHG-QIR
B-AChBP_T2	IAFHVSHG-QIR
L-AChBP_T1	WIVQACLS-LDR
L-AChBP_T2	WIVQGCLS-LDR
nAChR_h-A2	TEDRLFKHLFRGYNRWARPVPNTSDVVIVRFGLSIAQLIDVDEKNQMMTTNVWLKQ
nAChR_h-A4	TRAHAEERLLKKLFSGYNKWSRPVANISDVVLVRFGLSIAQLIDVDEKNQMMTTNVWVKQ
nAChR_h-A5	SIAKHEDSLLKDLFQDYERWVRPVEHLNDKIKIKFGLAISQLVDVDEKNQLMTTNVWLKQ
nAChR_h-A3	AEHRLFERLFEDYNEIIRPVANVSDPVIIHFEVSMSQLVKVDEVNQIMETNLWLKQ
nAChR_h-A6	TEERLFHKLFSHYNQFIRPVENVSDPVTVHFEVAITQLANVDEVNQIMETNLWLRH
nAChR_h-A1	HETRLVAKLFKDYSSVVRPVEDHRQVVEVTVGLQLIQLINVDEVNQIVTTNVRLKQ
nAChR_h-A7	KLYKELVKNYNPLERPVANDSQPLTVYFSLSLLQIMDVDEKNQVLTTNIWLQM
nAChR_h-A9	KLFNDLFEDYSNALRPVEDTDKVLNVTLQITLSQIKDMDERNQILTAYLWIRQ
B-AChBP_T1	WTLLNQITGESDVIPLSN-NTPLNVSLNFKLMNIVEADTEKDQVEVVLWTQA
B~AChBP_T2	WTLLNQITGESDVIPLSN-NTPLNVSLNFKLMNILEADTEKDQVEVVLWTQA
L-AChBP_T1	ADILYNIRQTSRPDVIPTQR-DRPVAVSVSLKFINILEVNEITNEVDVVFWQQT
L-AChBP_T2	ADILYNIRQTSRPDVIPTQR-DRPVAVSVSLKFINILEVNEITNEVDVVFWQQT
	
nAChR_h-A2	EWSDYKLRWNPTDFGNITSLRVPSEMIWIPDIVLYNNADGEFAVTHMTKAHLFSTGTVHW
nAChR_h-A4	EWHDYKLRWDPADYENVTSIRIPSELIWRPDIVLYNNADGDFAVTHLTKAHLFHDGRVQW
nAChR_h-A5	EWIDVKLRWNPDDYGGIKVIRVPSDSVWTPDIVLFDNADGRFEGTS-TKTVIRYNGTVTW
nAChR h-A3	IWNDYKLKWNPSDYGGAEFMRVPAQKIWKPDIVLYNNAVGDFQVDDKTKALLKYTGEVTW
nAChR h-A6	IWNDYKLRWDPMEYDGIETLRVPADKIWKPDIVLYNNAVGDFQVEGKTKALLKYNGMITW
nAChR h-A1	QWVDYNLKWNPDDYGGVKKIHIPSEKIWRPDLVLYNNADGDFAIVKFTKVLLQYTGHITW
nAChR h-A7	SWTDHYLQWNVSEYPGVKTVRFPDGQIWKPDILLYNSADERFDATFHTNVLVNSSGHCQY
nAChR h-A9	IWHDAYLTWDRDQYDGLDSIRIPSDLVWRPDIVLYNKADDESSEPVNTNVVLRYDGLITW
B-AChBP T1	SWKVPYYSS-LLSSSSLDQVSLPVSKMWTPDLSFYN-AIAAPELLSADRVVVSKDGSVIY
B-AChBP T2	SWKVPYYSS-LLSSSSLDQVSLPASKMWTPDLSFYN-AIAAPELLSTDRVVVSKDGSVIY
L-AChBP_T1	TWSDRTLAWNSSHSPDQVSVPISSLWVPDLAAYN-AISKPEVLTPQLARVVSDGEVLY
L-AChBP T2	TWSDRTLAWNSSHSPDQVSVPISSLWVPDLAAYN-AISKPEVLTPQLARVVSDGEVLY
-	- *
nAChR h-A2	VPPAIYKSSCSIDVTFFPFDQQNCKMKFGSWTYDKAKIDLEQMEQ-TVDLKDYWES-GEW
nAChR h-A4	TPPAIYKSSCSIDVTFFPFDQQNCTMKFGSWTYDKAKIDLVNMHS-RVDQLDFWES-GEW
nAChR h-A5	TPPANYKSSCTIDVTFFPFDLQNCSMKFGSWTYDGSQVDIILEDQ-DVDKRDFFDN-GEW
nAChR h-A3	IPPAIFKSSCKIDVTYFPFDYQNCTMKFGSWSYDKAKIDLVLIGS-SMNLKDYWES-GEW
nAChR h-A6	TPPAIFKSSCPMDITFFPFDHQNCSLKFGSWTYDKAEIDLLIIGS-KVDMNDFWEN-SEW
nAChR h-A1	TPPAIFKSYCEIIVTHFPFDEQNCSMKLGTWTYDGSVVAINPESD-QPDLSNFMES-GEW
nAChR h-A7	LPPGIFKSSCYIDVRWFPFDVQHCKLKFGSWSYGGWSLDLQMQ-EADISGYIPN-GEW
nAChR h-A9	DAPAITKSSCVVDVTYFPFDNQQCNLTFGSWTYNGNQVDIFNALD-SGDLSDFIED-VEW
B-AChBP T1	VPSORVRFTCDLINVDTEPG-ATCRIKVGSWTHDNKQFALITGEEGVVNIAEYFDS-PKF
B-AChBP T2	VPSQRVRFTCDLINVDTEPG-ATCRIKVGSWTFDNKQLALITGEEGVVNIAEYFDS-PKY
L-AChBP T1	MPSIRQRFSCDVSGVDTESG-ATCRIKIGSWTHHSREISVDPTTE-NSDDSEYFSQYSRF
L-AChBP T2	MPSIRQRFSCDVSGVDTESG-ATCRIKIGSWTHHSGEISVDPTTE-NSDDSEYFSQYSRF
	: * : * : : : :

Figure 4

(6/19)

nAChR h-A2	AIVNATGTYNSKKYDCCAE-IYPDVTYAFVIRRLPLFYTINLIIPCLLISCLTVLVFYLP
nAChR h-A4	VIVDAVGTYNTRKYECCAE-IYPDITYAFVIRRLPLFYTINLIIPCLLISCLTVLVFYLP
nAChR h-A5	EIVSATGSKGNRTDSCCWYPYVTYSFVIKRLPLFYTLFLIIPCIGLSFLTVLVFYLP
nAChR h-A3	
	AIIKAPGYKHDIKYNCCEE-IYPDITYSLYIRRLPLFYTINLIIPCLLISFLTVLVFYLP
nAChR_h-A6	EIIDASGYKHDIKYNCCEE-IYTDITYSFYIRRLPMFYTINLIIPCLFISFLTVLVFYLP
nAChR_h-A1	VIKESRGWKHSVTYSCCPDTPYLDITYHFVMQRLPLYFIVNVIIPCLLFSFLTGLVFYLP
nAChR_h-A7	DLVGIPGKRSERFYECCKE-PYPDVTFTVTMRRRTLYYGLNLLIPCVLISALALLVFLLP
nAChR_h-A9	EVHGMPAVKNVISYGCCSE-PYPDVTFTLLLKRRSSFYIVNLLIPCVLISFLAPLSFYLP
B-AChBP_T1	DLLSATQSLNRKKYSCCEN-MYDDIEITFAFRKK
B-AChBP_T2	DLLSATQSLNRKKYRCCEN-MYEDIEITFAFRKK
L-AChBP_T1	EILDVTQKKNSVTYSCCPE-AYEDVEVSLNFRKKGRSEIL
L-AChBP_T2	EILDVTQKKNSVIYSCCPE-AYEDVEVSLNFRKKGRSEIL
_	** * :::
nAChR h-A2	SDCGEKITLCISVLLSLTVFLLLITEIIPSTSLVIPLIGEYLLFTMIFVTLSIVITVFVL
nAChR h-A4	SECGEKITLCISVLLSLTVFLLLITEIIPSTSLVIPLIGEYLLFTMIFVTLSIVITVFVL
nAChR h-A5	SNEGEKICLCTSVLVSLTVFLLVIEEIIPSSSKVIPLIGEYLVFTMIFVTLSIMVTVFAI
nAChR h-A3	SDCGEKVTLCISVLLSLTVFLLVITETIPSTSLVIPLIGEYLLFTMIFVTLSIVITVFVL
nAChR h-A6	SDCGEKVTLCISVLLSLTVFLLVITETIPSTSLVVPLVGEYLLFTMIFVTLSIVVTVFVL
nAChR h-A1	TDSGEKMTLSISVLLSLTVFLLVIVELIPSTSSAVPLIGKYMLFTMVFVIASIIITVIVI
nAChR h-A7	ADSGEKISLGITVLLSLTVFMLLVAEIMPATSDSVPLIAQYFASTMIIVGLSVVVTVIVL
nAChR h-A9	AASGEKVSLGVTILLAMTVFQLMVAEIMP-ASENVPLIGKYYIATMALITASTALTIMVM
B-AChBP T1	
B-AChBP T2	
L-AChBP T1	
L-AChBP T2	
nAChR h-A2	NVHHRSPSTH-TMPHWVRGALLGCVPRWLLMNRP~
nAChR_h-A2 nAChR h-A4	NVHHRSPSTH-TMPHWVRGALLGCVPRWLLMNRP
nAChR_h-A4	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE
nAChR_h-A4 nAChR_h-A5	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T1	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T1	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T2	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T2 nAChR_h-A2	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T2 nAChR_h-A2 nAChR_h-A2 nAChR_h-A2 nAChR_h-A4	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T1 L-AChBP_T2 nAChR_h-A5	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T1 L-AChBP_T2 nAChR_h-A2 nAChR_h-A2 nAChR_h-A3	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T1 L-AChBP_T2 nAChR_h-A2 nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T1 L-AChBP_T2 nAChR_h-A2 nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A6 nAChR_h-A6 nAChR_h-A1	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T2 L-AChBP_T2 nAChR_h-A2 nAChR_h-A4 nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A1	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T2 L-AChBP_T2 nAChR_h-A2 nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A5 nAChR_h-A6 nAChR_h-A1 nAChR_h-A1 nAChR_h-A7 nAChR_h-A7	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 L-AChBP_T2 L-AChBP_T2 nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A1 nAChR_h-A7 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2 L-AChBP_T2 nAChR_h-A4 nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A7 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 B-AChBP_T2	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH
nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A6 nAChR_h-A1 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1 L-AChBP_T2 L-AChBP_T2 nAChR_h-A4 nAChR_h-A5 nAChR_h-A5 nAChR_h-A5 nAChR_h-A3 nAChR_h-A6 nAChR_h-A1 nAChR_h-A1 nAChR_h-A7 nAChR_h-A7 nAChR_h-A9 B-AChBP_T1	NVHHRSPRTH-TMPTWVRRVFLDIVPRLLLMKRPSVVKDNCRRLIESMHKMASAPRFWPE NIHHRSSSTHNAMAPLVRKIFLHTLPKLLCMRSH

Figure 4 (continued)

(7/19)

	·
nAChR h-A2	DRWACAGHVAPSVGTLCSHGHLHSGASGPKA
nAChR h-A4	PCRPPHGTQAPGLAKARSLSVQHMSSPGEAVEGGVRCRSRSIQYCVPRDDAAPEADGQAA
nAChR h-A5	
nAChR h-A3	DGMCGYCHHRRIKISNFSANLTRSSSSESVDA
nAChR h-A6	LKECFHCHKOPLOW
nAChR h-A1	KPGPPP
nAChR h-A7	GNLLYIGFRGLDGVHCVPTPDSGVVCGRMACSPTHD
nAChR h-A9	LKAARNKDLSRKKDMNKRLKNDLGCOGKNP
B-AChBP T1	DIVENTION VIOLENTIAN V
_	
B-AChBP_T2	
L-AChBP_T1	
L-AChBP_T2	
nAChR h-A2	EALLQEGELLLSPHMQKA
nAChR h-A4	GALASRNTHSAELPPPDQPSPCKCTCKKEPSSVSPSATVKTRSTKAPPPHLPLSPALTRA
nAChR h-A5	SRNTLEAA
nAChR h-A3	VLSLSALSPEIKEA
nAChR h-A6	VVENSEHSPEVEDV
nAChR_h-Al	MGFHSPLIKHPEVKSA
	EHLLHGGOPPEGDPDLAKI
nAChR_h-A7	- · · ·
nAChR_h-A9	QEAESYCAQYKVL
B-AChBP_T1	
B-AChBP_T2	
L-AChBP_T1	
L-AChBP_T2	
nAChR_h-A2	LEGVHYIADHLRSEDADSSVKEDWKYVAMVIDRIFLWLFIIVCFLGTIGLFLPPFLA
nAChR_h-A4	VEGVQYIADHLKAEDTDFSVKEDWKYVAMVIDRIFLWMFIIVCLLGTVGLFLPPWLA
nAChR_h-A5	LDSIRYITRHIMKENDVREVVEDWKFIAQVLDRMFLWTFLFVSIVGSLGLFVPVIYKWAN
nAChR_h-A3	IQSVKYIAENMKAQNEAKEIQDDWKYVAMVIDRIFLWVFTLVCILGTAGLFLQPLMA
nAChR_h-A6	INSVQFIAENMKSHNETKEVEDDWKYVAMVVDRVFLWVFIIVCVFGTAGLFLQPLLG
nAChR_h-A1	IEGIKYIAETMKSDQESNNAAAEWKYVAMVMDHILLGVFMLVCIIGTLAVFAGRLIE
nAChR h-A7	LEEVRYIANRFRCQDESEAVCSEWKFAACVVDRLCLMAFSVFTIICTIGILMSAP-NFVE
nAChR h-A9	TRNIEYIAKCLKDHKATNSKGSEWKKVAKVIDRFFMWIFFIMVFVMTILIIA
B-AChBP T1	
B-AChBP T2	
L-AChBP T1	
L-AChBP T2	
_	
nAChR h-A2	GMI
nAChR h-A4	GMI
nAChR h-A5	ILIPVHIGNANK
nAChR h-A3	REDA
nAChR h-A6	NTGKS
nAChR h-A1	LNQQG
nAChR h-A7	AVSKDFA
nAChR h-A9	AASUDIA
B-AChBP T1	
B-AChBP_T1 B-AChBP_T2	
L-AChBP_T1	
L-AChBP_T2	

Figure 4 (continued)

(8/19)

B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human	-MAELRRIILLCTIAFHVSHG-QIRWTLLNQITGESDVIPLSNNT-PLNVSLNFKLM -MAELRGIILLCTIAFHVSHG-QIRWTLLNQITGESDVIPLSNNT-PLNVSLNFKLMMRRNIFCLACLWIVQACLS-LDRADILYNIRQTSRPDVIPTQRDR-PVAVSVSLKFIMRRNIFCLACLWIVQGCLS-LDRADILYNIRQTSRPDVIPTQRDR-PVAVSVSLKFIMEPWPLLLLFSLCSAGLVLGSEHETRLVAKLFKDYSSVVRPVEDHRQVVEVTVGLQLI
A7_human	MRCSPGGVWLGLAASLLHVSLQGEFQRKLYKELVKNYNPLERPVANDSQPLTVYFSLSLL : : : * . : : : : : : :
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	NIVEADTEKDQVEVVLWTQASWKVPYYSS-LLSSSSLDQVSLPVSKMWTPDLSFYN-AIA NILEADTEKDQVEVVLWTQASWKVPYYSS-LLSSSSLDQVSLPASKMWTPDLSFYN-AIA NILEVNEITNEVDVVFWQQTTWSDRTLAWNSSHSPDQVSVPISSLWVPDLAAYN-AIS NILEVNEITNEVDVVFWQQTTWSDRTLAWNSSHSPDQVSVPISSLWVPDLAAYN-AIS QLINVDEVNQIVTTNVRLKQQWVDYNLKWNPDDYGGVKKIHIPSEKIWRPDLVLYNNADG QIMDVDEKNQVLTTNIWLQMSWTDHYLQWNVSEYPGVKTVRFPDGQIWKPDILLYNSADE ::::::::::::::::::::::::::::::::::::
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	APELLSADRVVVSKDGSVIYVPSQRVRFTCDLINVDTEPG-ATCRIKVGSWTHDNKQFAL APELLSTDRVVVSKDGSVIYVPSQRVRFTCDLINVDTEPG-ATCRIKVGSWTFDNKQLAL KPEVLTPQLARVVSDGEVLYMPSIRQRFSCDVSGVDTESG-ATCRIKIGSWTHHSREISV KPEVLTPQLARVVSDGEVLYMPSIRQRFSCDVSGVDTESG-ATCRIKIGSWTHHSGEISV DFAIVKFTKVLLQYTGHITWTPPAIFKSYCEIIVTHFPFDEQNCSMKLGTWYDGSVVAI RFDATFHTNVLVNSSGHCQYLPPGIFKSSCYIDVRWFPFDVQHCKLKFGSWSYGGWSL .: * : * : * : * : * : * : * : * : * : *
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	ITGEEGVVNIAEYFDS-PKFDLLSATQSLNRKKYSCC-ENMYDDIEITFAFRKK ITGEEGVVNIAEYFDS-PKYDLLSATQSLNRKKYRCC-ENMYEDIEITFAFRKK DPTTE-NSDDSEYFSQYSRFEILDVTQKKNSVTYSCC-PEAYEDVEVSLNFRKKGRSEIL DPTTE-NSDDSEYFSQYSRFEILDVTQKKNSVIYSCC-PEAYEDVEVSLNFRKKGRSEIL NPESD-QPDLSNFMES-GEWVIKESRGWKHSVTYSCCPDTPYLDITYHFVMQRLPLYFIV DLQMQ-EADISGYIPN-GEWDLVGIPGKRSERFYECC-KEPYPDVTFTVTMRRRTLYYGL : :::::::::::::::::::::::::::::::::::
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	NVIIPCLLFSFLTGLVFYLPTDSGEKMTLSISVLLSLTVFLLVIVELIPSTSSAVPLIGK NLLIPCVLISALALLVFLLPADSGEKISLGITVLLSLTVFMLLVAEIMPATSDSVPLIAQ
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	YMLFTMVFVIASIIITVIVINTHHRSPSTHVMPNWVRKVFIDTIPNIMFFSTMKRPSREK YFASTMIIVGLSVVVTVIVLQYHHHDPDGGKMPKWTRVILLNWCAWFLRMKRPGEDK
B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	QPPMGVRPACQHKQRRCSLASVEMSAVGPPPASNGNLLYIGFRGLDGVHCVPTPDSGVVCGRMAC

Figure 5

(9/19)

B-AChBP_T1. B-AChBP_T2. L-AChBP_T1. L-AChBP_T2. A1_human A7_human	FHSPLIKHPEVKSAIEGIKYIAETMKSDQESNNAAAEWKYVAMVMDHILL SPTHDEHLLHGGQPPEGDPDLAKILEEVRYIANRFRCQDESEAVCSEWKFAACVVDRLCL
B-AChBP T1.	
B-AChBP T2.	
L-AChBP T1.	
L-AChBP T2.	
A1_human	GVFMLVCIIGTLAVFAGRLIELNQQG
A7_human	MAFSVFTIICTIGILMSAPNFVEAVSKDFAZ

Figure 5 (continued)

(10/19)

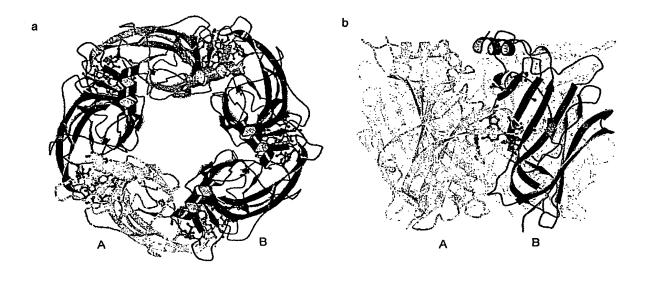
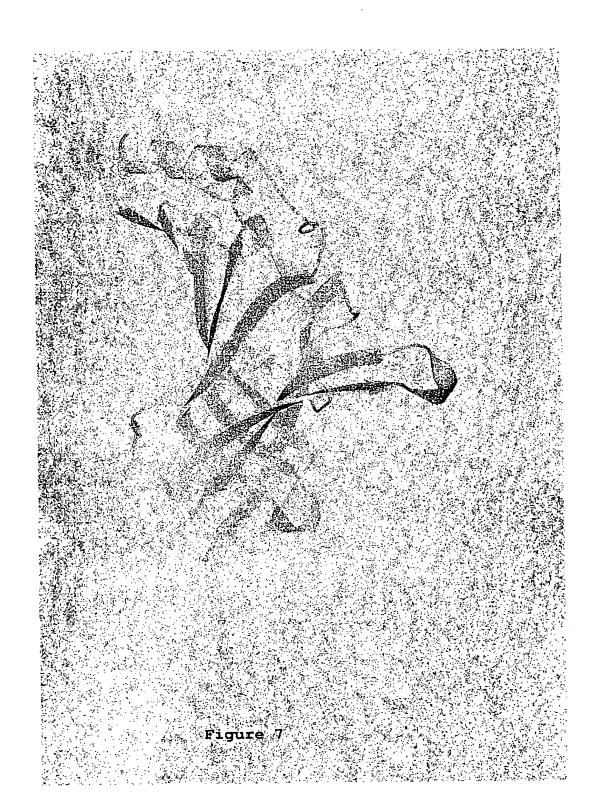
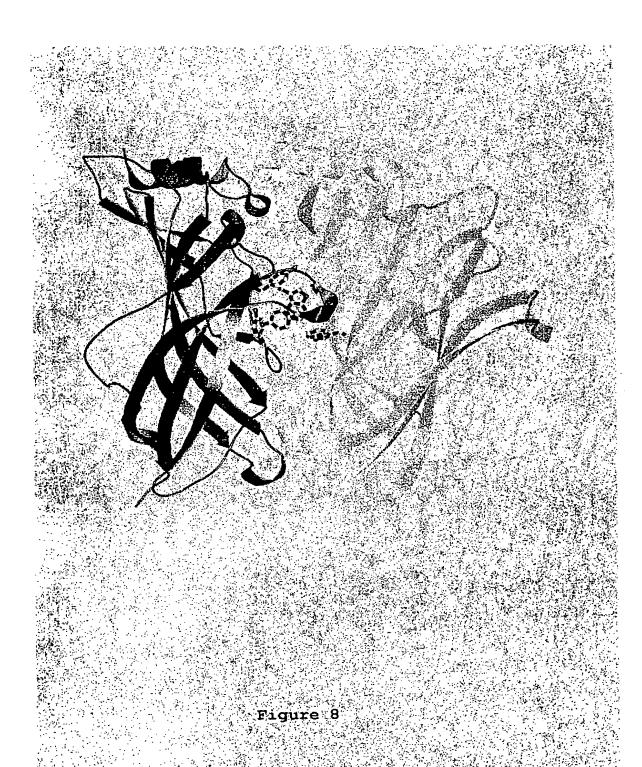


Figure 6

(11/19)



(12/19)



(13/19)

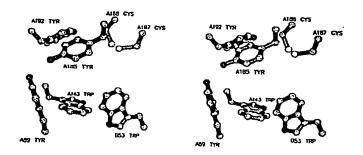


Figure 9

(14/19)

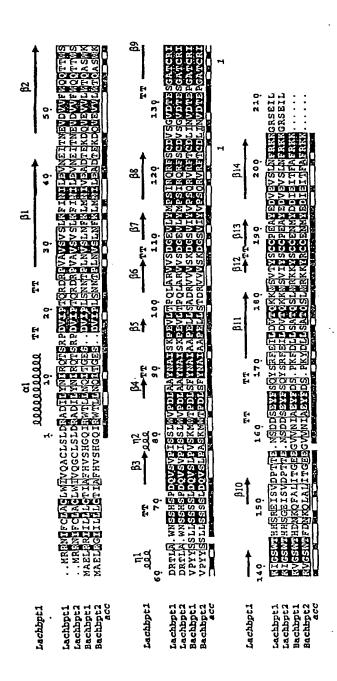


Figure 10

(15/19)

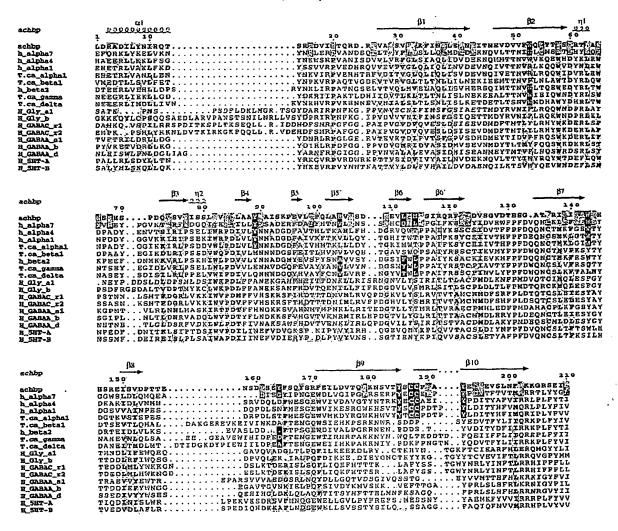


Figure 11

(16/19)

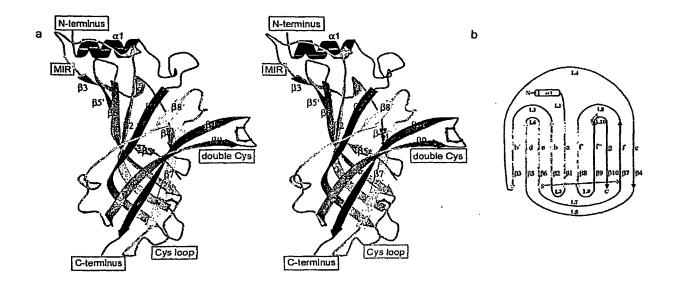


Figure 12

(17/19)

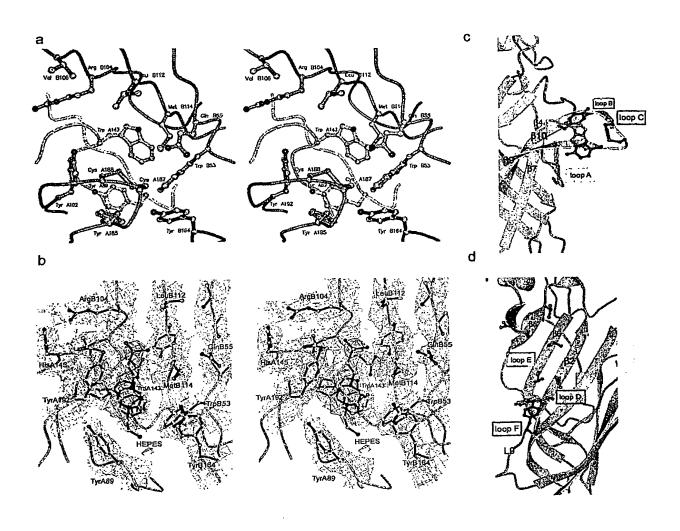


Figure 13

(18/19)

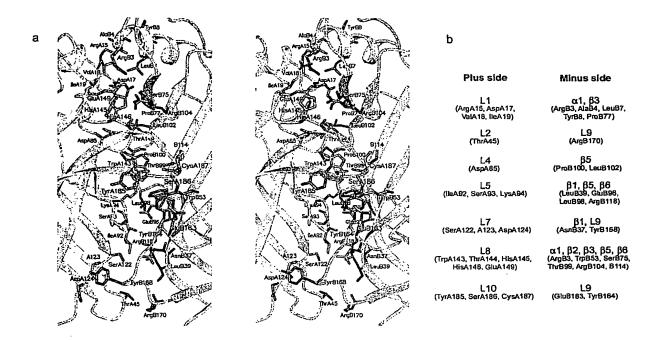


Figure 14

(19/19)

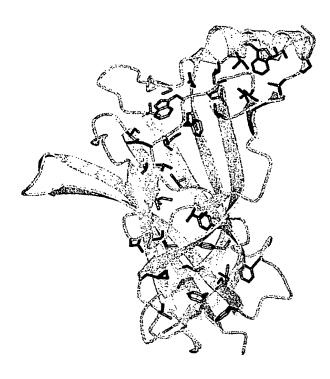


Figure 15

(1/20)

SEQUENCE LISTING

<110> Stichting voor de Technische Wetenschappen

<120> Water-soluble ligand-binding proteins and analogs of ligand-gated ion channels, crystals thereof and their use for screening ligands of ligand-gated ion channels

```
<130> F 1105 PCT
<140>
<141>
<160> 20
<170> PatentIn Ver. 2.1
<210> 1
<211> 690
<212> DNA
<213> Lymnaea stagnalis
<220>
<221> CDS
<222> (1)..(687)
<220>
<221> mat_peptide
<222> (58)..(687)
<400> 1
```

atg cgt cga aac att ttc tgc ctt gct tgt ctc tgg atc gtg caa gcg 48
Met Arg Arg Asn Ile Phe Cys Leu Ala Cys Leu Trp Ile Val Gln Ala
-15 -10 -5

tgt cta agc ttg gac cgg gca gac atc ttg tac aac ata cgt cag aca 96

Cys Leu Ser Leu Asp Arg Ala Asp Ile Leu Tyr Asn Ile Arg Gln Thr

-1 1 5 10

(2/20)

teg	aga	ccg	gat	gtg	att	ccc	aca	cag	cga	gat	cgc	cca	gtg	gcg	gtg	144
Ser	Arg	Pro	Asp	Val	Ile	Pro	Thr	Gln	Arg	Asp	Arg	Pro	Val	Ala	Val	
	15					20					25					•
tcc	gtc	tct	ttg	aag	ttc	atc	aac	atc	ttg	gaa	gtg	aat	gaa	ata	acc	192
Ser	Val	Ser	Leu	Lys	Phe	Ile	Asn	Ile	Leu	Glu	Val	Asn	Glu	Ile	Thr	
30					35					40					45	
aat	gaa	gtg	gac	gtg	gtc	ttt	tgg	cag	cag	acg	aca	tgg	tcg	gac	agg	240
Asn	Glu	Val	qaA	Val	Val	Phe	Trp	Gln	Gln	Thr	Thr	Trp	Ser	Asp	Arg	
				50					55					60		
acc	ctc	gcc	tgg	aac	agt	tct	cac	tca	cca	gat	cag	gtt	tcc	gtg	cca	288
Thr	Leu	Ala	Trp	Asn	Ser	Ser	His	Ser	Pro	Asp	Gln	Val	Ser	Val	Pro	
			65					70		_			75			
ata	agc	tct	tta	tgg	ata	cct	gac	ctc	act	gca	tac	aac	gcc	atc	tcg	336
	_		_	Trp					-				-			
		80					85				-3-	90				
aaa	cct	gaa	atc	ctt	aca	cca	caa	cta	acc	agg	atc	ata	tcc	gat	agt	384
		-	-	Leu		-			_		_					
	95					100				5	105				4	
	,,															
naa	ata	cta	tac	atg	cca	agt	atc	cac	cag	caa	ttc	tee	tac	gat	ota	432
-		_		Met	_	_		_	_				_	_		
110	142	Lou	-1.		115			9		120			- , -		125	
					110											
tca	aat	atc	αat	acg	gag	tcc	aat	act	aca	tat	caa	atc	222	att	aat:	480
-		-	_	Thr	_		_		_			_		_		•
501	013	VUL	nap	130	Olu	OCL	013		135	C, 5	1129		2,5	140	0_3	
				130					133					110		
tcc	taa	acc	Cac	cac	art	ana	gag	att	tet	orta	cat-	ccc	aca	aca	gaa	528
				His												320
Ser	ııp	1111	145	nis	Ser	мg	Giu	150	Ser	var	Asp	rio	155	1111	GIG	
			143					±30					100			
22+	a~+	~~+	α -+	tct	as s	tec	++-	taa	car	tec	tot		+++	ma a	ato	576
	_	-	-	Ser	_							_				310
ASA	Sel		Asp	ser	GIU	тУт		Set	Gitti	TÄT	Ser		FIIE	GIU	116	
		160	•				165					170				

(3/20)

ttg	gac	gtc	aca	cag	aag	aag	aac	tcg	gtt	acc	tac	tct	tgc	tgt	ccg	624
Leu	Asp	Val	Thr	Gln	Lys	Lys	Asn	Ser	Val	Thr	Tyr	Ser	Cys	Суз	Pro	
	175					180					185					•
gag	gca	tac	gag	gac	gtt	gaa	gtg	agt	ctc	aat	ttc	cgg	aag	aag	gga	672
Glu	Ala	Tyr	Glu	Asp	Val	Glu	Val	Ser	Leu	Asn	Phe	Arg	Lys	Lys	Gly	
190					195					200					205	
cgc	tcc	gaa	att	ctt	tag								•		•	690
Arg	Ser	Glu	Ile	Leu												
				210												
<21	0> 2															
<21	1> 2:	29														
<21	2> PI	RT														
<21	3> Ly	ymna	ea si	tagna	alis											
<40	0> 2															
Met	Arg	Arg	Asn	Ile	Phe	Cvs	Leu	Ala	Cvs	Leu	Tro	Tle	Va l	Gln	Δla	
	_	_		-15		-			-10				142	-5	1114	
														J		
Cys	Leu	Ser	Leu	Asp	Arg	Ala	Asp	Tle	Len	ጥኒታ	Δen	Tle	Ara	Gln	mh∽	
_		-1	1		3		5		LCu	+3-	71011	10	ALG	GIII	1 111.	
		_	_				J					Τ.0				
Ser	Ara	Pro	Asp	Val	Ile	Pro	ሞb v	G1n	λνα	y an	7~~	Dwa	1703	71-	TT- 3	
	15			741	220	20	1111	GIII	ALG	nsp		PLO	vai	Ala	vaı	
						20					25					
Ser	Val	Ser	T.e.u	Lve	Phe	Tlo	λen	Tlo	T ON	~1	*** 1	3	01	-1 -	m1	
30	,	501	Dea	Ly S	35	116	Maii	116	ьец		vai	Asn	GIU	тте		
50					33					40					45	
Acn	Clu	Wa I	A ===	7707	*** 3	Db =		61	~ 1	mı.			_			
nsii	GIU	vai	Asp		Val	Pne	Trp	GIN		Thr	Thr	Trp	Ser		Arg	
				50					55					60		
Mh w	T 0	21-	m	3	a -			_	_	_						
1111	ьец	АТА		ASII	Ser	ser	Hls		Pro	Asp	GIn	Val		Val	Pro	
			65					70					75			
	_	_	_	_		_										
тте	ser		Leu	Trp	Val	Pro		Leu	Ala	Ala	Tyr	Asn	Ala	Ile	Ser	
		80					85					90				

(4/20)

Lys Pro Glu Val Leu Thr Pro Gln Leu Ala Arg Val Val Ser Asp Gly 95 100 105

Glu Val Leu Tyr Met Pro Ser Ile Arg Gln Arg Phe Ser Cys Asp Val 110 120 125

Ser Gly Val Asp Thr Glu Ser Gly Ala Thr Cys Arg Ile Lys Ile Gly 130 135 140

Ser Trp Thr His His Ser Arg Glu Ile Ser Val Asp Pro Thr Thr Glu 145 150 155

Asn Ser Asp Asp Ser Glu Tyr Phe Ser Gln Tyr Ser Arg Phe Glu Ile 160 165 170

Leu Asp Val Thr Gln Lys Lys Asn Ser Val Thr Tyr Ser Cys Cys Pro 175 180 185

Glu Ala Tyr Glu Asp Val Glu Val Ser Leu Asn Phe Arg Lys Lys Gly
190 200 205

Arg Ser Glu Ile Leu 210

<210> 3

<211> 690

<212> DNA

<213> Lymnaea stagnalis

<220>

<221> CDS

<222> (1)..(687)

<220>

<221> mat_peptide

<222> (58)..(687)

<400> 3

(5/20)

ıtg	cgt	cga	aac	att	ttc	tgc	ctt	gct	tgt	ctc	tgg	atc	gtg	caa	ggg	48
ſet	Arg	Arg	Asn	Ile	Phe	Cys	Leu	Ala	Cys	Leu	Trp	Ile	Val	Gln	Gly	
				-15					-10					~5		
gt	cta	agc	ttg	gac	cgg	gca	gac	atc	ttg	tac	aac	ata	cgt	cag	aca	96
:ys	Leu	Ser	Leu	Asp	Arg	Ala	Asp	Ile	Leu	Tyr	Asn	Ile	Arg	Gln	Thr	
		-1	1				5					10				
.cg	aga	ccg	gat	gtg	att	ccc	aca	cag	cga	gat	cgc	cca	gtg	gcg	gtg	144
er	Arg	Pro	Asp	Val	Ile	Pro	Thr	Gln	Arg	Asp	Arg	Pro	Val	Ala	Val	
	15		_			20			_	-	25					
cc	gtc	tct	ttg	aag	ttc	atc	aac	atc	ttg	gaa	gtg	aat	gaa	ata	acc	192
			_	Lys					_	_			-			
30					35					40	•				45	
at	gaa	ata	gac	gtg	ata	tet	t aa	cag	cag	acq	aca	taa	tca	gac	agg	240
				Val				_	_	_			_	_		
1011	O_u	V CL	ASD	50	Val	1110	115	GIII	55	1111	1111	TID	DCI	60	ALG.	
				50					33					00		
	ctc	aaa	+ ~ ~	aac	aat	tat	020	taa	cca	ant.	aaa	~++	taa	ata	cca	288
		_		Asn	_					_	_	_				200
. 111	Deu	nia	65	NSII	per	Ser	UTS	70	FLO	ASD	GIII	Vai	75	VAI	FIO	
			0.5					, 0					73			
				.											.	226
	_		_	tgg			_			_			_			336
тe	ser		ьеи	Trp	vaı	Pro		ьец	Ата	AIA	туг		Ата	ire	ser	
		80					85					90				
																- 0
		-	_	ctt				_	_		-	_		-		384
ıys		GIu	Val	Leu	Thr		Gin	Leu	Ala	Arg		Val	Ser	Asp	Gly	
	95					100					105					
				atg										_		432
31u	Val	Leu	Tyr	Met	Pro	Ser	Ile	Arg	Gln	Arg	Phe	Ser	Суз	Asp	Val	
L10					115					120					125	
cg	ggt	gtc	gat	acg	gag	tcc	ggt	gct	acg	tgt	cgg	atc	aaa	att	ggt	480
Ser	Gly	Val	Asp	Thr	Glu	Ser	Gly	Ala	Thr	Cys	Arg	Ile	Lys	Ile	Gly	
				130					135					140		

(6/20)

					_	-				_	_		_	aca Thr	•	528
		_										_		gaa Glu		576
		-	_		_				_				_	tgt Cys	_	624
				-	_	-		-					-	aag Lys		672
_		_	att Ile	ctt Leu 210	tag											690
<211 <211	0> 4 1> 2: 2> Pl 3> Ly	RT	ea st	tagna	alis								·			
	0> 4 Arg	Arg	Asn	Ile -15	Phe	Суз	Leu	Ala	Cys -10	Leu	Trp	Ile	Val	Gln -5	Gly	
Сув	Leu	Ser -1	Leu 1	Asp	Arg	Ala	Asp 5	Ile	Lėu	Tyr	Asn	Ile 10	Arg	Gln	Thr	
Ser	Arg 15	Pro	Asp	Val	Ile	Pro 20	Thr	Glņ	Arg	Asp	Arg 25	Pro	Val	Ala	Val	
Ser 30	Val	Ser	Leu	Lys	Phe 35	Ile	Asn	Ile	Leu	Glu 40	Val	Asn	Glu	Ile	Thr 45	

(7/20)

50

55

60

Thr Leu Ala Trp Asn Ser Ser His Ser Pro Asp Gln Val Ser Val Pro
65 70 75

Ile Ser Ser Leu Trp Val Pro Asp Leu Ala Ala Tyr Asn Ala Ile Ser 80 85 90

Lys Pro Glu Val Leu Thr Pro Gln Leu Ala Arg Val Val Ser Asp Gly 95 100 105

Ser Gly Val Asp Thr Glu Ser Gly Ala Thr Cys Arg Ile Lys Ile Gly 130 135 140

Ser Trp Thr His His Ser Gly Glu Ile Ser Val Asp Pro Thr Thr Glu 145 150 155

Asn Ser Asp Asp Ser Glu Tyr Phe Ser Gln Tyr Ser Arg Phe Glu Ile 160 165 170

Leu Asp Val Thr Gln Lys Lys Asn Ser Val Ile Tyr Ser Cys Cys Pro 175 180 185

Glu Ala Tyr Glu Asp Val Glu Val Ser Leu Asn Phe Arg Lys Lys Gly
190 195 200 200

Arg Ser Glu Ile Leu

210

<210> 5

<211> 675

<212> DNA

<213> Bulinus truncatus

<220>

(8/20)

<221>	- CD	S														
<222	· (1) (672)	•												
<220	>															
_		t pe	ptid	le												
	_		(672													
	()	4 ,	(0,2	,												
<400	> 5															
atg (gct	gaa	cta	cga	agg	atc	att	ctt	ctg	cta	tgt	act	att.	gcc	ttt	48
Met i	Ala	Glu	Leu	Arg	Arg	Ile	Ile	Leu	Leu	Leu	Cys	Thr	Ile	Ala	Phe	
	-20					-15					-10					
cat (gtt	tcc	cat	gga	caa	ata	aga	tgg	acg	ctg	ctg	aat	cag	atc	acc	96
His '	Val	Ser	His	Gly	Gln	Ile	Arg	Trp	Thr	Leu	Leu	Asn	Gln	Ile	Thr	
~5				-1	1				5					10		
ggt	gaa	tct	gac	gtc	att	ccg	ctg	tct	aac	aac	acg	ccc	ctg	aat	gtg	144
G1y	Glu	Ser	Asp	Val	Ile	Pro	Leu	Ser	Asn	Asn	Thr	Pro	Leu	Asn	Val	
			15					20					25			
tcg	ctg	aat	ttt	aag	ctg	atg	aat	atc	gta	gag	gcg	gac	aca	gaa	aaa	192
Ser	Leu	Asn	Phe	Lys	Leu	Met	Asn	Ile	Val	Glu	Ala	qaA	Thr	Glu	Lys	
		30					35					40				
gat	caa	gtg	gag	gtc	gtg	ctg	tgg	aca	cag	gct	agc	tgg	aaa	gtg	ccg	240
qaA	Gln	Val	Glu	Val	Val	Leu	Trp	Thr	Gln	Ala	Ser	Trp	Lys	Val	Pro	
	45					50					55					
														agc		288
Tyr	Tyr	Ser	Ser	Leu	Leu	Ser	Ser	Ser	Ser	Leu	Asp	Gln	Val	Ser		
60					65					70					75	
														gcc		336
Pro	Val	Ser	Lys	Met	Trp	Thr	Pro	Asp	Leu	Ser	Phe	Tyr	Asn	Ala		
				80)				85					90		
												_				201
														aag		384
Ala	Ala	Pro	Glu	Lev	ı Lev	. Ser	Ala			r Val	. Val	Val		. Lys	Asp	
			95	j.				100)				105	•		

(9/20)

199	age	gte	acc	tac	gtc	CCC	ayc	cag	agg	gcc	cgc	CCC	acc	cyc	gue	
Зlу	Ser	Val	Ile	Tyr	Val	Pro	Ser	Gln	Arg	Val	Arg	Phe	Thr	Суз	Asp	
		110					115					120				
ett	att	aat	gtc	gac	acq	gag	cca	gga	gcc	acc	tgt	cgc	atc	aaa	gtc	480
			Val													
eu.		ASII	vai	Asp	TILL		110	013	niu			••••		_,,		
	125					130					135					
									L	~		252		~~~	~2 ~	528
			acc													320
Gly	Ser	Trp	Thr	His	Asp	Asn	Lys	Gln	Phe	Ala	Leu	Tie	Thr	GIĀ		
140					145					150					155	
gag	ggg	gtg	gtg	aat	att	gca	gag	tac	ttc	gac	agc	cca	aag	ttt	gac	576
Glu	Gly	Val	Val	Asn	Ile	Ala	Glu	Tyr	Phe	Asp	Ser	Pro	Гуs	Phe	qaA	
				160					165					170		
ctt	tta	agt	gcc	aca	cag	agt	ctg	aat	cgc	aag	aag	tac	agc	tgt	tgc	624
			Ala													
пси	Dea	DCL			U-22			180		-	-	_	185			
			175					100								
					~~~	a + +	~22	2++	200	+++	aca	ttc	aga	aag	aag	672
																• •
Glu	Asn	Met	Tyr	Asp	Asp	TIE			inr	Pne	Ата			цуз	цуs	
		190	)				195					200				
taa																675
<21	.0> <del>6</del>	5														
<21	.1> 2	224														
_	.2> I															
			nus t		+116											
<21	.37 [	20111	ius (	, L UII	Jacus	•										
- 4 (		_														
	)0> (		_			1.	1.	- T-,		. T.O.	. (	n mha	r T1a	. Δ1 <i>.</i>	Phe	
Met			и ьег	ı Ar	g Arg			s rie	Thec	ı ne					a Phe	
	-20	0				-1	)				-10	J				
							•			-	_		- 63		. mb	
Hi	s Va	l Se	r Hi	s Gl	y Gl	n Il	e Ar	g Tr			u Lei	ı Ası	n Gli		e Thr	
-	5			-	1	1				5				1	U	
Gl	y Gl	u Se	r As	p Va	1 11	e Pr	o Le	u Se	r Ası	n As	n Th	r Pr	o Le	u As	n Val	

(10/20)

15 20 25

Ser Leu Asn Phe Lys Leu Met Asn Ile Val Glu Ala Asp Thr Glu Lys
30 35 40

______

Asp Gln Val Glu Val Val Leu Trp Thr Gln Ala Ser Trp Lys Val Pro 45 50 55 .

Tyr Tyr Ser Ser Leu Leu Ser Ser Ser Ser Leu Asp Gln Val Ser Leu 60 70 75

Pro Val Ser Lys Met Trp Thr Pro Asp Leu Ser Phe Tyr Asn Ala Ile
80 85 90

Ala Ala Pro Glu Leu Leu Ser Ala Asp Arg Val Val Val Ser Lys Asp 95 100 105

Gly Ser Val Ile Tyr Val Pro Ser Gln Arg Val Arg Phe Thr Cys Asp 110 115 120

Leu Ile Asn Val Asp Thr Glu Pro Gly Ala Thr Cys Arg Ile Lys Val 125 130 135

Glu Gly Val Val Asn Ile Ala Glu Tyr Phe Asp Ser Pro Lys Phe Asp 160 165 170

Leu Leu Ser Ala Thr Gln Ser Leu Asn Arg Lys Lys Tyr Ser Cys Cys
175 180 185 .

Glu Asn Met Tyr Asp Asp Ile Glu Ile Thr Phe Ala Phe Arg Lys Lys
190 195 200

<210> 7

<211> 675

<212> DNA

# (11/20)

<213	<213> Bulinus truncatus															
<220	>															
<221	> CD	s														
<222	> (1	) (	672)													
<220	>															
<221	> ma	t_pe	ptid	e												
<222	> (6	4)	(672	)												
<400	> 7															
atg	gct	gaa	cta	cga	ggg	atc	att	ctt	ctg	cta	tgt	act	att	gcc	ttt	48
Met	Ala	Glu	Leu	Arg	Gly	Ile	Ile	Leu	Leu	Leu	Cys	Thr	Ile	Ala	Phe	
	-20					-15					-10					
cat	gtt	tcc	cat	gga	caa	ata	aga	tgg	acg	ctg	ctg	aat	cag	atc	acc	96
														Ile		
-5				-1	1				5					10		
ggt	gaa	tct	gac	gtc	att	ccg	ctg	tct	aac	aac	acg	cca	ctg	aat	gtg	144
														Asn		
_			15					20					25			
tcg	ctg	aat	ttt	aag	ctg	atg	aat	atc	tta	gag	gcg	gac	aca	gag	aaa	192
_														Glu		
		30					35					40				
gat	caa	gtg	gag	gtc	gtg	ctg	tgg	aca	cag	gct	agc	tgg	aaa	gtg	ccg	240
														Val		
	45					50					55		-			
tat	tac	agc	tca	ctg	ctg	tcc	tct	agc	agt	tta	gac	cag	gtg	agc	tta	288
Tyr	Tyr	Ser	Ser	Leu	Leu	Ser	Ser	Ser	Ser	Leu	Asp	Gln	Val	Ser	Leu	
60					65					70	)				75	
								·								*
сса	gcc	agc	aaa	atg	tgg	acc	сса	gac	ctt	tct	ttc	tat	aac	gcc	atc	336
Pro	Ala	Ser	Lys	Met	Trp	Thr	Pro	asp	Leu	Ser	Phe	Tyr	Asr	Ala	Ile	
				80					85					90		
	•															
gct	gca	ccc	gag	, ttg	cto	tcc	aca	gac	cgc	gto	ggtg	gto	tct	aag	gac	384

### (12/20)

Ala	Ala	Pro	Glu	Leu	Leu	Ser	Thr	qaA	Arg	Val	Val	Val	Ser	Lys	Asp	
			95					100					105			
																•
ggg	agc	gtc	att	tac	gtg	ccc	agc	cag	agg	gtc	cgt	ttc	acc	tgc	gac	432
											Arg					
		110					115					120				
ctt	att	aat	gtg	gac	acg	gag	ccg	gga	gcc	acc	tgt	cgc	atc	aaa	gtc	480
											Cys					
	125			_		130					135					
gga	tcc	taa	acc	ttc	gac	aac	aaa	cag	ctc	gcc	ctg	atc	acc	ggg	gag	528
											Leu					
140					145					150					155	
aaa	aaa	ata	ata	aat	att	gca	gag	tac	ttc	gac	agc	cca	aag	tac	gac	576
Glu	Glv	Val	val	Asn	Ile	Ala	Glu	Tyr	Phe	Asp	Ser	Pro	Lys	Туг	Asp	
Giu	. 017	102	•	160	_			_	165					170		
art	++0	aat	acc	aca	cag	agt	cto	aat	cgc	aag	, aag	tac	aga	tgt	tgc	624
															. Cys	
пес	. Dec		. 175		0.2			180					185			
			. 1/5	•												
	<b></b>		. + a +		, dad	att	· gaa	att	acc	: ttt	gca	tto	aga	aaa	g aag	672
gaç	, aai	. acc	- mar	. gac	. gac	. T] e	- Gli	ı Ile	e Thi	. Phe	e Ala	. Phe	Arg	g Ly:	s Lys	
GI1	1 ASI	1 Me		. Gr			19					200				
		191	J													
<b>.</b>	_															675
ta	a															
_		_														
	10>															
	11>															
	12>		<b></b> -	+ ~···~	cativ	c										
<2	13>	Rull	nus	cr un	catu											
. 4																
/	1107	*														

His Val Ser His Gly Gln Ile Arg Trp Thr Leu Leu Asn Gln Ile Thr

Met Ala Glu Leu Arg Gly Ile Ile Leu Leu Cys Thr Ile Ala Phe

-15

-10

# (13/20)

-5				-1	1				5					10	
Gly	Glu	Ser	Asp 15	Val	Ile	Pro	Leu	Ser 20	Asn	Asn	Thr	Pro	Leu 25	Asn	Val
Ser	Leu	Asn 30	Phe	Lys	Leu	Met	Asn 35	Ile	Leи	Glu	Ala	Asp 40	Thr	Glu	Lys
Asp	Gln 45	Val	Glu	Val	Val	Leu 50	Trp	Thr	Gln	Ala	Ser 55	Trp	Lys	Val	Pro
Tyr 60	Tyr	Ser	Ser	Leu	Leu 65	Ser	Ser	Ser	Ser	Leu 70	Asp	Gln	Val	Ser	Leu 75
Pro	Ala	Ser	Lys	Met 80	Trp	Thr	Pro	qaA	Leu 85	Ser	Phe	Tyr	Asn	Ala 90	Ile
Ala	Ala	Pro	Glu 95	Leu	Leu	Ser	Thr	Asp 100	Arg	Val	Val	Val	Ser 105	Lys	Asp
Gly	Ser	Val 110	Ile	Tyr	Val	Pro	Ser 115	Gln	Arg	Val	Arg	Phe 120	Thr	Cys	Asp
Leu	Ile 125	Asn	Val	Asp	Thr	Glu 130	Pro	Gly	Ala	Thr	Cys 135	Arg	Ile	Ъуs	Val
Gly 140	Ser	Trp	Thr	Phe	Asp 145	Asn	Lys	Gln	Leu	Ala 150		Ile	Thr	Gly	Glu 155
Glu	Gly	Val	Val	Asn 160		Ala	Glu	Туг	Phe 165		Ser	Pro	Lys	Туг 170	
Leu	Leu	Ser	Ala 175		Gln	Ser	Leu	Asn 180		Lys	Lys	Туг	Arg 185		Cys
Glu	Asn	Met 190		Glu	Asp	Ile	: Glu 195		. Thr	Phe	e Ala	200		Lys	. Lys

(14/20)

<210>	> 9														
<211>	> 50	2						•							
<212	> PR	T													
<213	> Ho	mo s	apie	ns											
<220	>														
<221	> DO	MAIN													
<222	> (1	) (	235)												
,															
<400	> 9			•											
Met :	Arg	Сув	Ser	Pro	Gly	Gly	Val	Trp	Leu	Ala	Leu	Ala	Ala	Ser	Leu
1				5					10					15	
Leu	His	Val	Ser	Leu	Gln	Gly	Glu	Phe	Gln	Arg	Lys	Leu		Lys	Glu
			20					25					30		
												_ •	_		<b>G</b>
Leu	Va1	Lys	Asn	Tyr	Asn	Pro		Glu	Arg	Pro	Val		Asn	Asp	ser
		35					40					45			
							_	_	_	_	<b>.</b>	<b>0</b> 3	T7 -	M-+	7 ~~
Gln		Leu	Thr	Val	Tyr		Ser	Leu	Ser	ьеи		GIN	тте	mec	Asp
	50					55					60				
	_			3	Q1	770 T	T 011	Ωh ∽	Φh.~	λεν	Tle	רדיניים	T.OU	Gln	Met
	Asp	Glu	гуѕ	ASN		Vai	ьеи	1111	1111	75	110	LLD	дси	022	80
65					70					, 3					
g	<b></b>	Thr	7 ~~	uic	The area	Leu	Gln	Ψ×n	Asn	Val	Ser	Glu	Tvr	Pro	Gly
ser	Trp	THE	Asp	85		Dea	GLII	115	90	*42	20.		-2-	95	
				03	•										
Val.	Tave	Thr	Val	Ara	Phe	Pro	Asp	Gly	Gln	Ile	Trp	Lys	Pro	Asp	Ile
Val	<b>-</b> 27.5	1111	100	2-2-9				105			_	_	110		
Leu	Leu	Tvr	Asn	Ser	Ala	Asp	Glu	Arg	Phe	Asp	Ala	Thr	Phe	His	Thr
		115				_	120					125			
Asn	Val	Leu	Val	Asn	Ser	Ser	Gly	His	Cys	Gln	Tyr	Leu	Pro	Pro	Gly
	130					135					140				

Ile Phe Lys Ser Ser Cys Tyr Ile Asp Val Arg Trp Phe Pro Phe Asp

155

150

145

### (15/20)

Val	Gln	His	Суз	Lys 165	Leu	Lys	Phe	Gly	Ser 170	Trp	Ser	Tyr	Gly	Gly 175	Trp
Ser	Leu	Asp	Leu	Gln	Met	Gln	Glu	Ala	Asp	Ile	Ser	Gly	Tyr	Ile	Pro
501			180	3233				185	-			-	190		
Asn	Gly	Glu 195	Trp	Asp	Leu	Val	Gly 200	Ile	Pro	Gly	Lys	Arg 205	Ser	Glu	Arg
Phe	Tyr 210	Glu	Cys	Cys	Lys	Glu 215	Pro	Tyr	Pro	Asp	Val 220	Thr	Phe	Thr	Val
Thr 225	Met	Arg	Arg	Arg	Thr 230	Leu	Tyr	Tyr	Gly	Leu 235	Asn	Leu	Leu	Ile	Pro 240
Сув	Val	Leu	Ile	Ser 245	Ala	Leu	Ala	Leu	Leu 250	Val	Phe	Leu	Leu	Pro 255	Ala
Asp	Ser	Gly	Glu 260		Ile	Ser	Leu	Gly 265	Ile	Thr	Val	Leu	Leu 270	Ser	Leu
Thr	Val	Phe 275		Leu	Leu	Val	Ala 280		Ile	Met	Pro	Ala 285	Thr	Ser	Asp
Ser	Val		Leu	ı Ile	Ala	Gln 295		Phe	Ala	Ser	Thr		Ile	Ile	Val
Gly 305		ı Ser	Val	. Val	. Val		· Val	Ile	e Val	. Leu 315		Tyr	His	His	His 320
Ası	Pro	o Ası	9 Gl	7 Gly 325	/ Lys	Met	: Pro	Lys	330		Arg	Val	Ile	. Leu 335	
Ası	ת מינו	o Cvi	s Ala	a Tri	o Phe	. Lei	ı Arç	g Met	: Lys	a Arg	g Pro	Gly	glu	ı Asp	Lys

345

Val Arg Pro Ala Cys Gln His Lys Gln Arg Arg Cys Ser Leu Ala Ser 360

Val Glu Met Ser Ala Val Ala Pro Pro Pro Ala Ser Asn Gly Asn Leu

340

355

350

(16/20)

380

370 375

Leu Tyr Ile Gly Phe Arg Gly Leu Asp Gly Val His Cys Val Pro Thr 385 390 395 400

Pro Asp Ser Gly Val Val Cys Gly Arg Met Ala Cys Ser Pro Thr His 405 410 415

Asp Glu His Leu Leu His Gly Gly Gln Pro Pro Glu Gly Asp Pro Asp 420 425 430

Leu Ala Lys Ile Leu Glu Glu Val Arg Tyr Ile Ala Asn Arg Phe Arg 435 440 445

Cys Gln Asp Glu Ser Glu Ala Val Cys Ser Glu Trp Lys Phe Ala Ala 450 455 460

Cys Val Val Asp Arg Leu Cys Leu Met Ala Phe Ser Val Phe Thr Ile 465 470 475 480

Ile Cys Thr Ile Gly Ile Leu Met Ser Ala Pro Asn Phe Val Glu Ala 485 490 495

Val Ser Lys Asp Phe Ala 500

<210> 10

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: N-terminus of mature LAChBP1

<400> 10

Leu Asp Arg Ala Asp Ile Leu Tyr Asn Ile

(17/20)

```
<210> 11
<211> 32
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:
      Oligonucleotides encoding N-terminal peptide of
      LAChBP1
<220>
<221> modified_base
<222> (13)
<223> i
<400> 11
                                                                    32
cggatccgay mgagcngaya thytntayaa ya
 <210> 12
 <211> 31
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> Description of Artificial Sequence: Primer1 useful
       for cloning cDNA encoding LAChBP (optionally with
       Primer2)
 <220>
 <221> modified_base
 <222> (14)
 <223> i
  <220>
 <221> modified_base
  <222> (20)
  <223> i
```

<400> 12

(18/20)

```
31
gcgaattcga yacagarwsa ggngcnacnt g
<210> 13
<211> 33
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer2
      useful for cloning cDNA encoding LAChBP
      (optionally with Primer1)
<220>
<221> modified_base
<222> (20)
<223> i
<400> 13
                                                                    33
gcgaagette rtcytertaa gcytengere are
 <210> 14
 <211> 9
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> Description of Artificial Sequence: His-tag
 <400> 14
 Ser Arg Gly His His His His His
                   5
   1
 <210> 15
 <211> 14
 <212> PRT
 <213> Artificial Sequence
```

#### (19/20)

```
<220>
<223> Description of Artificial Sequence: His-tag
Glu Phe Lys Asp Asp Asp Lys His His His His His
                  5
<210> 16
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Additional
      amino acids at the N-terminus of mature LAChBP due
      to alpha-mating factor cleavage site
<400> 16
Glu Ala Glu Ala
  1
<210> 17
<211> 47
<212> DNA
<213> Artificial Sequence
 <220>
 <223> Description of Artificial Sequence: Primer useful
       for generating LAChBP/alpha7 nAChR chimera
 <400> 17
                                                                   47
 gcgctcgaga aaagagaggc tgaagctttg gaccgggcag acatctt
 <210> 18
 <211> 30
```

<212> DNA

# (20/20)

213> Artificial Sequence	
<220>	
<223> Description of Artificial Sequence: Primer useful	
for generating LAChBP/alpha7 nACHR chimera	
<400> 18	30
cgcgaattca agaatttcgg agcgtccctt	30
<210> 19	
<211> 42	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> Description of Artificial Sequence: Primer useful	
for generating LAChBP/alpha7 nACHR chimera	
400. 10	
<pre>&lt;400&gt; 19 gtggaaacca gacattctcc tctacaacgc catctcgaaa cc</pre>	42
gtggaaacca gacattetee tetacaacge carregam	
<210> 20	
<211> 39	
<212> DNA	•
<213> Artificial Sequence	
<220>	
<223> Description of Artificial Sequence: Primer useful	
for generating LAChBP/alpha7 nACHR chimera	
<400> 20	
gaggagaatg tetggtttee acaaagaget tattggeae	. 39
anadanana no caa an a	